"THE PREVALENCE OF HYPOTHYROIDISM IN PATIENTS WITH PROVEN GALL STONE DISEASE"

Dissertation submitted by

DR. PRETHEE MARTINA CHRISTABEL

In partial fulfilment of the requirements for

MASTER OF SURGERY
IN
GENERAL SURGERY
May 2019

Done under the guidance of

Dr. T.S. BALASHANMUGAM

Professor of Surgery

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Coimbatore – 641004

DECLARATION

I, **Dr.PRETHEE MARTINA CHRISTABEL**, solemnly declare that this dissertation **"THE PREVALENCE OF HYPOTHYROIDISM IN PATIENTS WITH PROVEN GALL STONE DISEASE"** is a bonafide record of work done by me in the Department of General Surgery, PSG institute of Medical Sciences & Research, Coimbatore, under the guidance of **Dr.T.S.BALASHANMUGAM**, Professor of Surgery.

This dissertation is submitted to The Tamilnadu Dr.M.G.R. Medical University, Chennai, in partial fulfillment of the University regulations for the award of MS Degree (General Surgery) Branch-I, Examination to be held in May 2019.

(Dr.PRETHEE MARTINA CHRISTABEL)

Place: Coimbatore

Date:

CERTIFICATE BY THE GUIDE

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This is to certify that this dissertation entitled **"THE PREVALENCE OF HYPOTHYROIDISM IN PATIENTS WITH PROVEN GALL STONE DISEASE"** is a record of bonafide research work done by **Dr.PRETHEE MARTINA CHRISTABEL** , under the guidance of Dr.T. S. BALASHANMUGAM , Professor, Department of General Surgery, PSG Institute of Medical Sciences and Research, Coimbatore– 641004.

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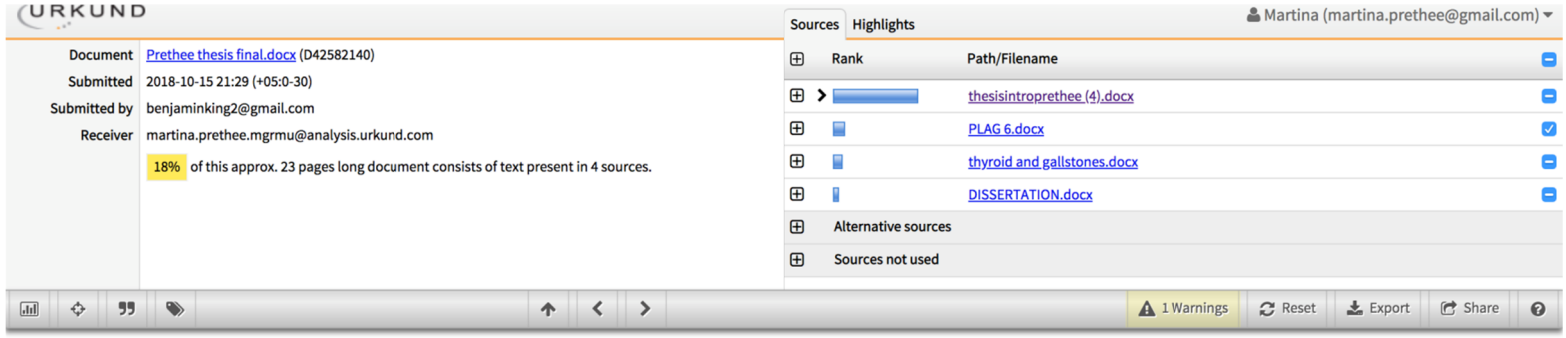

The Prevalence of Hypothyroidism in patients with proven Gall stone disease

This dissertation is submitted to PSG Institute of Medical Sciences and Research in partial fulfilment of the regulations for the M.S (General Surgery) Degree Examination, April 2019

By

Dr. PRETHEE MARTINA CHRISTABEL

Done under the guidance of

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DECLARATION

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To
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Department of General Surgery
Guide: Dr T S Balashanmugam
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Coimbatore 641 004

Ref: Project No.16/353

Date: October 24, 2016

Dear Dr Prethee,

Institutional Human Ethics Committee, PSG IMS&R reviewed and discussed your application dated 18.10.2016 to conduct the research study entitled "*Prevalence of hypothyroidism in patients with proven gall stone disease in PSG Hospitals*" during the IHEC meeting held on 21.10.2016.

The following documents were reviewed and approved:

1. Project submission form
2. Study protocol (Version 1 dated 18.10.2016)
3. Informed consent forms (Version 1 dated 18.10.2016)
4. Data collection tool (Version 1 dated 18.10.2016)
5. Permission letter from concerned Head of the Department
6. Current CVs of Principal investigator, Co-investigator
7. Budget

The following members of the Institutional Human Ethics Committee (IHEC) were present at the meeting held on 21.10.2016 at IHEC Secretariat, PSG IMS & R between 10.00 am and 11.00 am:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Mr R Nandakumar (Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes
2	Dr. S. Bhuvaneshwari (Member-Secretary, IHEC)	MD	Clinical Pharmacology	Female	Yes	Yes
3	Dr S Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
4	Dr Sudha Ramalingam	MD	Epidemiologist, Ethicist Alt. member-Secretary	Female	Yes	Yes
5	Dr D Vijaya	M Sc., Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes

The study is approved in its presented form. The decision was arrived at through consensus. Neither PI nor any of proposed study team members were present during the decision making of the IHEC. The IHEC functions in accordance with the ICH-GCP/ICMR/Schedule Y guidelines. The approval is valid until one year from the date of sanction. You may make a written request for renewal / extension of the validity, along with the submission of status report as decided by the IHEC.

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Following points must be noted:

1. IHEC should be informed of the date of initiation of the study
2. Status report of the study should be submitted to the IHEC every 12 months
3. PI and other investigators should co-operate fully with IHEC, who will monitor the trial from time to time
4. At the time of PI's retirement/intention to leave the institute, study responsibility should be transferred to a colleague after obtaining clearance from HOD, Status report, including accounts details should be submitted to IHEC and extramural sponsors
5. In case of any new information or any SAE, which could affect any study, must be informed to IHEC and sponsors. The PI should report SAEs occurred for IHEC approved studies within 7 days of the occurrence of the SAE. If the SAE is 'Death', the IHEC Secretariat will receive the SAE reporting form within 24 hours of the occurrence
6. In the event of any protocol amendments, IHEC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. Alteration in the budgetary status should be clearly indicated and the revised budget form should be submitted
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval
   d. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented
   e. If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IHEC and only then can they be implemented
   f. Any deviation-Violation/waiver in the protocol must be informed to the IHEC within the stipulated period for review
7. Final report along with summary of findings and presentations/publications if any on closure of the study should be submitted to IHEC

Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

Thanking You,

Yours Sincerely,

SECRETARY
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COIMBATORE-641004
INSTITUTIONAL HUMAN ETHICS COMMITTEE

Dr S Bhuvaneshwari
Member - Secretary
Institutional Human Ethics Committee

INTRODUCTION

1. Introduction

Gall stone disease is one of the most common gastro intestinal pathologies causing significant morbidity and mortality. The prevalence of gall stone disease in India varies widely with a 2-4 fold higher prevalence among North Indians compared to south Indian population. The composition of stone varies as well with Cholesterol stones predominantly seen in the western population and pigment stones seen in Asian and Indian population. Pigment stones are predominant in south Indian population. Gallstones may be single or multiple. Depending on their composition they may be radio lucent or radio opaque. Supersaturation of cholesterol in bile in the nucleation process leading to the formation of cholesterol crystals is an important step in the formation of bile stones. Biliary stasis and infection also play an important role in the formation of pigment stones. Sphincter of Oddi , hepatic clearance of bile and several other mechanical factors contribute to the formation of gall stones.

Thyroid hormone deficiency is also widely prevalent and is usually sub clinical and goes undetected for decreased. There is an overlap of the population in which both gall stone disease and hypothyroidism are common owing to several factors in thyroid hormone action which influence the formation of gall stone disease. Several studies have established role of thyroid hormone in cholesterol metabolism. It is a contributing factor to dyslipidemia. Thyroid hormone and the presence of Thyroxine receptors in the sphincter of oddi caus-

es a pro relaxant effect of on the sphincter . The reduced levels of thyroid hormone leads to increased sphincter pressures and biliary stasis. These factors all contribute to biliary stasis in Hypothyroid patients. Estimating the prevalence of hypothyroidism in patients with gall stone disease could further help correlate the association between hypothyroidism in gall stone disease.

AIM AND OBJECTIVES

Aim: To study the prevalence of clinical and sub clinical hypothyroidism in patients with proven gall stone disease.

OBJECTIVE:

- To study the prevalence of hypothyroidism in patients with proven gall stone disease

- To see whether there is significant prevalence of hyporthyroidism among patients with proven gall stone disease

REVIEW OF LITERATURE

BILIARY SYSTEM ANATOMY:

The biliary system consists of intra and extra hepatic biliary trees which act as a storage for bile and which empties into the duodenum. The segmental ducts join to form the bile canaliculi which fuse at ports hepatic to form right and left hepatic ducts which continue as extra hepatic portal system. [1,2]

GALLBLADDER

The gallbladder is a flask like organ on the inferior surface of the liver, it empties into the common bile duct through the cystic duct. It has a storage capacity of 30-50ml and is usually 8-10cm long. It lies in the fall bladder fossa of the liver parenchyma covered by the peritoneum. This attachment can vary widely. The position and size of the gall bladder within the gall bladder fossa may vary anatomically. The Gall bladder consists of a neck , infundibulum, body and fundus. The porta hepatis is medial to the neck and anterior to the second part of duodenum. In the neck, medially there is an oblique ridge in the mucosa which is continuous as the spiral valve of cystic duct. Laterally it widens to form the 'Hartmann's pouch'. [1,2]

The body is in contact with the gall bladder fossa on the inferior surface of the liver. The fundus projects past the inferior border of the liver laterally and is the anterior abdominal wall at the mid clavicular line near the tip of the ninth costal cartilage. This point is usually tender in inflammatory pathologies of the gall bladder and is known in clinical examination as Murphy's point. [1,2]

The fundus may be folded back upon the body of the gall bladder to form the Phrygian cap . In rare cases there may be congenital anomalies associated with gall bladder anatomy such as bifid gall bladder .

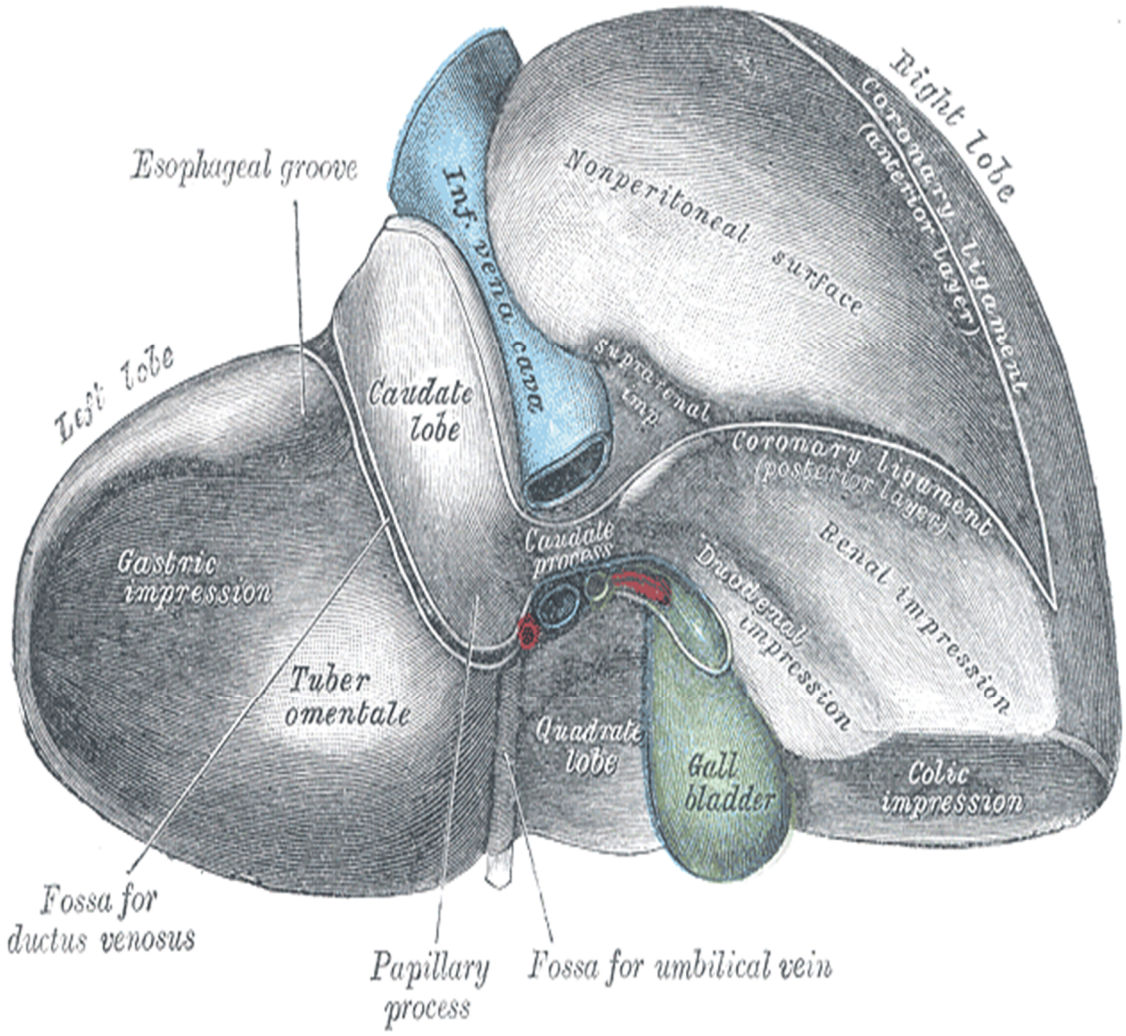


Fig 1 : Gall bladder and its anatomical relations.

CALOT'S TRIANGLE

The Calot's triangle is the triangular space, formed between, the common hepatic duct , the cystic duct and the inferior surface of segment V of the liver. It is a pyramidal 'space' with one apex lying at the porta hepatis, one at the junc-

tion of the cystic duct and fundus of the gallbladder, and two closer apices at the attachments of the gallbladder to the liver bed. The base of the triangle is formed by the inferior surface of the liver. The cystic artery, the cystic lymph node (Node of Lund) and lymphatics from the gallbladder, one or two small cystic veins, the autonomic nerves running to the gallbladder, and some loose adipose tissue all lie within the Calot's Triangle. It may contain accessory ducts which drain from the liver into the gallbladder. [3]

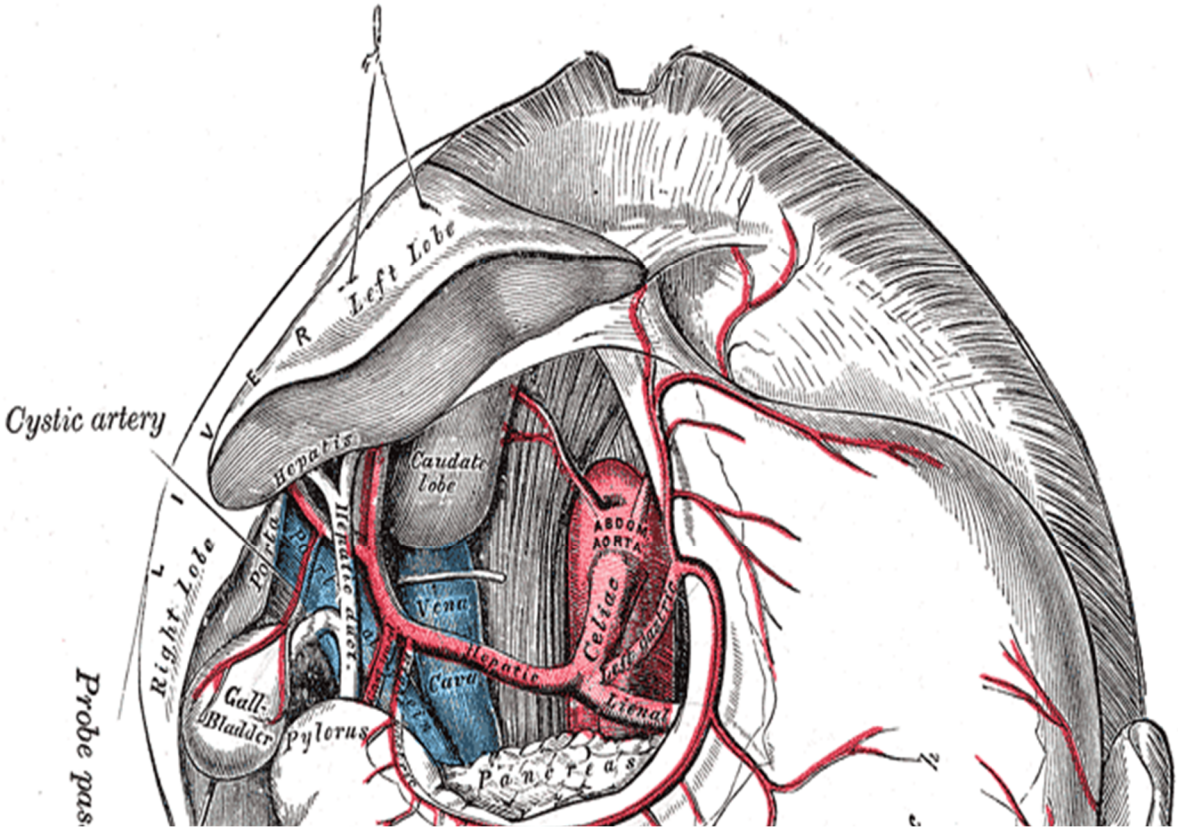


Figure 2 : Calot's Triangle

CYSTIC DUCT

The cystic duct is 3-4 cms in length. The Gall bladder drains into the common bile duct via the Cystic duct. It lies posterior to the neck of the gall bladder and passes left to drain into the common hepatic duct . This is continued as the common bile duct. The cystic duct runs parallel to the common hepatic duct for a short distance before joining it. [3]

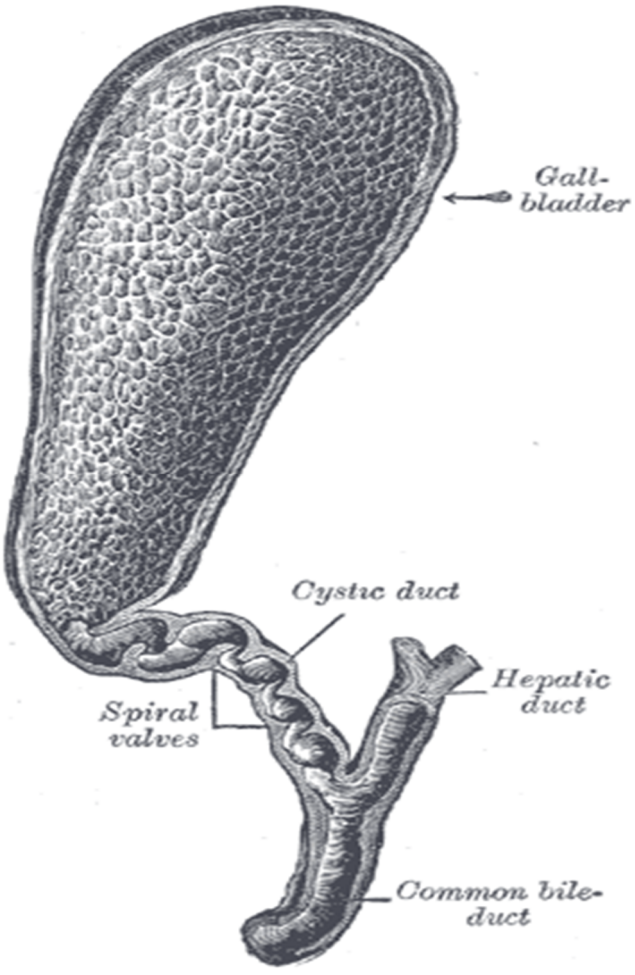


Fig 3: Gall bladder and cystic duct

The position of the cystic duct is widely varied in its anatomy. The cystic duct can lie anterior or posterior to the common hepatic duct, In some cases an elongated cut can drain directly into the Right hepatic duct. There may be a double cystic duct or an absent cystic duct. Accessory hepatic ducts arising from segment V of the liver may join either the right hepatic duct, common hepatic duct, the common bile duct, the cystic duct or the gall bladder directly. These anatomical variations should be considered during surgical excision of the gall bladder. Care must be taken during clipping or legation of cystic duct to preserve the common bile duct and to clip accessory ducts which may be mistaken for Right or common hepatic duct. [3]

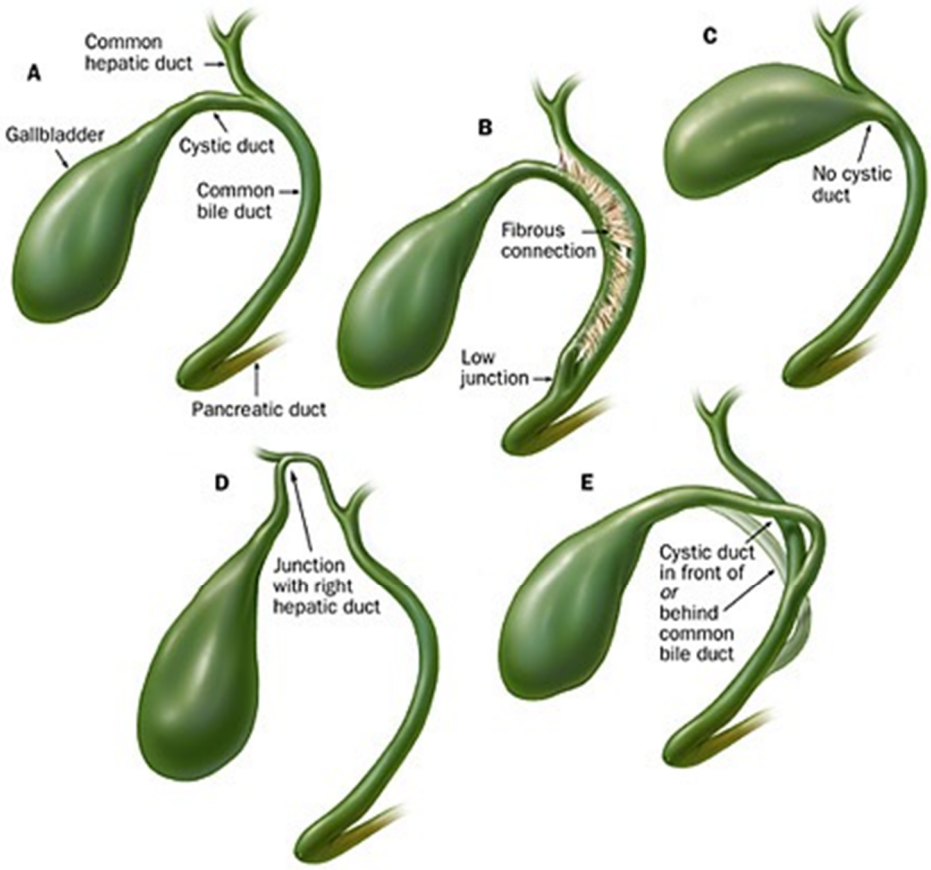


Fig 4: Cystic duct and it variations.

HEPATIC BILE DUCTS

The Right and left hepatic ducts arise form the liver and join to form the Common hepatic duct near the porta hepatis. The Right hepatic duct, is short and vertical while the left, is horizontal and lies in

segment IV. The Cystic duct joins the common hepatic duct on its right to form the CBD. [3]

COMMON BILE DUCT

The cystic and common hepatic ducts join to form the common bile duct near the porta hepatis.

The length is between 6 and 8 cm and diameter is around 4.1 mm . A diameter of more than 8mm is considered abnormal . It is anatomically divided into ,

A. Supra duodenal Part

Supra duodenal part in the free margin of lesser omentum.

1. Anteriorly: Liver.
2. Posteriorly: Portal vein and epiploic foramen.
3. To the left: Hepatic artery

B. Retro duodenal Part

1. Anteriorly: First part of duodenum.
2. Posteriorly: Inferior vena cava.
3. To the left: Gastro duodenal artery.

C. Infra duodenal Part

1. Anteriorly: A groove in the upper and lateral parts posterior to the head of the pancreas.

2. Posteriorly: Inferior vena cava.

D. Intra duodenal Part

The IVC lies posterior to the duct and the duct may be occasionally embedded in the pancreatic tissue. [3]

HEPATOPANCREATIC AMPULLA (OF VATER)

The common bile duct and the main pancreatic duct unites extrinsic to the duodenal wall and traverses the wall of the duodenum as a single duct. In about 20% of the population , they join within the duodenal wall and have a short or no common bile duct, and can have a common opening into the duodenum. In about 10% of the population they open via separate openings in the duodenum. The lower part of the common bile duct and the terminal part of the main pancreatic duct are surrounded by circular muscle fibers forming the bile duct and the pancreatic duct sphincter and hepatic pancreatic ampulla (Sphincter of Oddi) respectively. This apparatus allows for control of pancreatic and common bile duct emptying.[2,3]

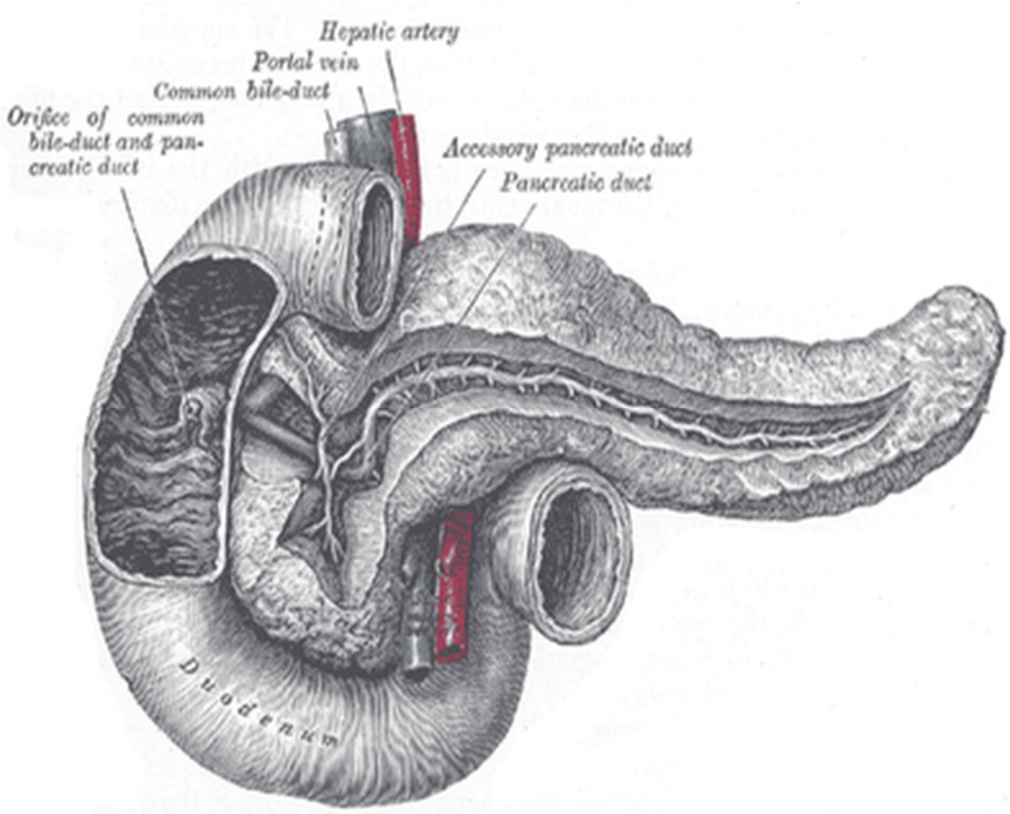


Figure 5 : Ampulla of Vater

VASCULAR SUPPLY OF THE GALL BLADDER AND BILIARY TRACT :

CYSTIC ARTERY

Cystic artery derives its origin from the Right hepatic artery. The cystic artery is the chief source of the blood supply, and is distributed to the gall bladder, the cystic duct, the hepatic ducts and the upper part of the bile duct . Several branches from the posterior superior pancreatic duodenal artery supply the lower part of the bile duct. The right hepatic artery forms a minor source of supply to the middle part of the bile duct.

The cystic artery passes behind the common hepatic and cystic ducts, and reaches the upper surface of the neck of the gall bladder, where it divides into superficial and deep branches.

The origin of the cystic artery varies anatomically , the commonest variation is arising from the Common hepatic artery. It may arise from Left hepatic , Gastro duodenal, rarely superior Pancreatico-duodenal, right gastric, Coeliac and Superior mesenteric arteries. Accessory cystic artery can arise from the common hepatic artery and it may also give rise to an additional branch before it enters the Gall bladder. The variants of cystic artery usually pass anterior to the common hepatic duct or the Bile duct to reach the Gall bladder.[5] In intrahepatic Gall bladder multiple blood supply is derived from multiple branches from the parenchyma of Segments IV or V . Occlusion of the cystic artery does not directly led to necrosis due to the varying blood supply. [4]

DUCTAL ARTERIES :

A fine network of vessels supply the common bile duct and hepatic ducts which close to the ducts. Disruption of this network of vessels during surgical exposure of the bile ducts frequently causes chronic ischemia and stenosis of the duct. The common bile duct is usually supplied by two to

four ascending and descending arteries which form long narrow anastomotic channels along the length of the duct which are usually divided into medial and lateral trunks. The largest contribution is usually from the retroduodenal branch of the gastroduodenal artery as it crosses the anterior surface of the duct at the

upper border of the duodenum. As they lie in close proximity to the lower common hepatic duct, they may form the dominant blood supply to the common bile duct. A Retro portal artery arising from the coeliac axis, superior mesenteric artery or one of their major branches runs upwards on the posterior surface of the portal vein they terminate by joining the Retro duodenal artery close to the lower end of the Supra duodenal Bile duct. [4]

CYSTIC VEINS

The superior surface of the body and neck of the gall bladder is drained by multiple small veins . The veins are present loose areolar tissue between the gall bladder and liver. They drain into the segmental portal veins. The rest of the Gall bladder is drained by one or two of the veins may form a small cystic vein which enters the liver either directly or after joining the veins that drain the hepatic ducts. The Bile duct is drained by veins which drain into the portal vein . [4]

LYMPHATICS:

Multiple lymphatic vessels run from the submucosal and subserosal plexuses of the gallbladder , cystic duct, common hepatic and upper part of common bile ducts. They drain into the cystic node, which usually lies above the cystic duct in the tissue of Calot's triangle and into a node lying in the anterior border of the free edge of the lesser omentum. The cystic node may be enlarged in acute cholecystitis. The lower part of the bile duct usually drains into the lower hepatic and upper pancreatic splenic nodes [3,4]

INNERVATION

The innervation of the gallbladder and the extra hepatic biliary tree is by branches from the hepatic plexus. The innervation of the retro duodenal part of the common bile duct and the smooth muscle of the hepatic pancreatic ampulla is from the pyloric branches of the vagi. Pain caused by stretch of the common bile duct or gallbladder is referred to the epigastrium in accordance with the origin of the foregut structures. Involvement of the somatic peritoneum produces pain which is localised to the right upper quadrant. [2,3]

GALLBLADDER

The gall bladder histologically consists of serosa, sub serosa and mucosa. It lacks a submucosa and muscular layer. The serosa covers the fundus, body and neck of the gallbladder. including the inferior surface Beneath the serosa is sub serosa . The mucosa is yellow brown with multiple rugae that resemble the intestinal villi. They flatten as the gall bladder distends with bile. The mucosa is composed of columnar cells with apical microvilli and spaces between the epithelial cells. It concentrates the bile by water and solute absorption which is facilitated by the rich network of capillaries beneath the basement membrane.. The fibromuscular layer consists of fibrous tissue and smooth muscle cells arranged in longitudinal, circular and oblique bundles. [6,7]

BILE DUCTS

The biliary ducts consists of inner mucosal layer and outer fibrous layer. The outer fibrous connective tissue layer is composed of a varying amount of longitudinal, oblique and circular smooth muscle cells. The mucosa consists of tubu-

lo alveolar mucous glands which are continuous with the mucosa of the gall bladder and intra hepatic ducts. [6,7]

SPHINCTER OF ODDI:

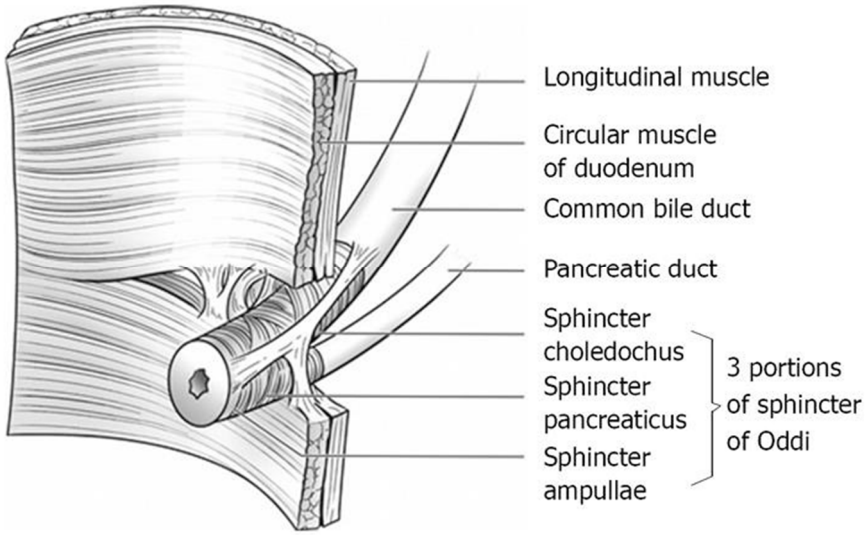


Figure 6 : Sphincter of Oddi

The sphincter of Oddi regulates the emptying of bile into the duodenum and prevents the regurgitation of duodenal contents back into the biliary tree. The musculature of the sphincter is functionally varied from the duodenal musculature. The sphincter of odds maintains a high basal pressure which is 3 mm Hg higher than the CBD or pancreas. It exhibits integrate contractions at the rate 4 per minute towards the duodenum. The contraction of relaxation of sphincter of oddi is influenced by many factors. In the fasting state it remains contracted The relaxation is under the action of Cholecystokinin and secretin.[11,12]

Vast active intestinal peptide also plays a role in relaxation of sphincter of oddi. Thyroxine exhibits a pro relaxant effect on the sphincter the absence of

which results in high sphincter pressures. The control of the sphincter is predominantly hormonal with the sphincter functioning even when denervated. [7]

PHYSIOLOGY OF THE BILIARY SYSTEM

Hepatocytes secrete bile into the biliary canaliculi at the rate of 1000 ml per day. The secreted bile facilitates absorption of fat by emulsifying the fat which is then lysed by the pancreatic lipase enzyme.

BILE SECRETION:

Bile is secreted in the liver in two stages :

1. The bile secreted into the canaliucli by the hepatocytes consists of

   a. Bile acids : Cholic and chenodeoxycholic acid

   b. Bile salts: They are formed by linking glycerine and taurine . They have hydrophobic and hydrophilic regions which enables them to emulsify fats. The bile salts are absorbed in the distal ileum .

   c. Bile pigments are a product of haemoglobin breakdown. They are bound to albumin and transported and are later conjugated with glucuronic acid . They are further broken down into uro billion and stercobilin

2. The bile flows in the canaliculi , empties into the terminal bile ducts and flows into the common hepatic duct and the common bile duct. During its course through the ducts is enriched with sodium and bicarbonate . [7]

STORAGE OF BILE*:*

40-50 ml of Bile can normally be stored in the gallbladder and can hold upto 500ml. The gallbladder mucosa are continually absorbs sodium , chloride, water and other electrolytes. Gall bladder concentrates bile upto 10

fold. During concentration , water and large portions of the electrolytes (except calcium ions) are reabsorbed by the gallbladder mucosa; except the bile salts and the lipid substances such as cholesterol and lecithin and hence become highly concentrated in the Gall bladder bile. This differentiates it from the intrahepatic bile. [2]

HORMONAL CONTROL OF BILE SECRETION

1. CHOLECYSTOKININ

Post prandial secretion of cholecystokinin stimulates contraction of all bladder and relaxation of sphincter of oddi and facilitates release of bile into the duodenum

2. SECRETIN

Secretin stimulates secretion of Sodium Bicarbonate from the gall bladder. This in turn helps to neutralise the Acid from the stomach. Apart of secretin , gastrin and glucagon also play an important role in hormonal control of bile secretion.

3. NEURAL CONTROL

Apart from hormonal control the secretion is also controlled by vague fibers. The vagal fibers stimulate contraction and the splanchnic sympathetic fibers inhibit motor activity. [9]

ENTEROHEPATIC CIRCULATION:

More than 90% of the bile salts are reabsorbed from the distal ileum and transported back to the liver through the portal vein. The absorption is predominantly by diffusion and by active transport processes in the detail ileal mucosa. They are transported back to the liver where they are absorbed completely in to the hepatocytes and re secreted into the biliary canaliculi again. The enterohepatic circulation recycles the bile around 17 times before being excreted in the faces or urine. [9]

GALLSTONE DISEASE

Galls stone disease is one of the most common pathology to affect the digestive tract. The incidence and prevalence of gall stones in related to many factors including age, gender, ethnic background and body mass index. Many factors such as obesity , pregnancy, Crohn's disease, hemolytic anemia are all associate with increased risk of gall stone formation. Hypothyroidism as evidenced by recent studies may also be associated with increased risk of gall stone formation. Female gender has three times increased incidence of galls tone disease compared to men. [9]

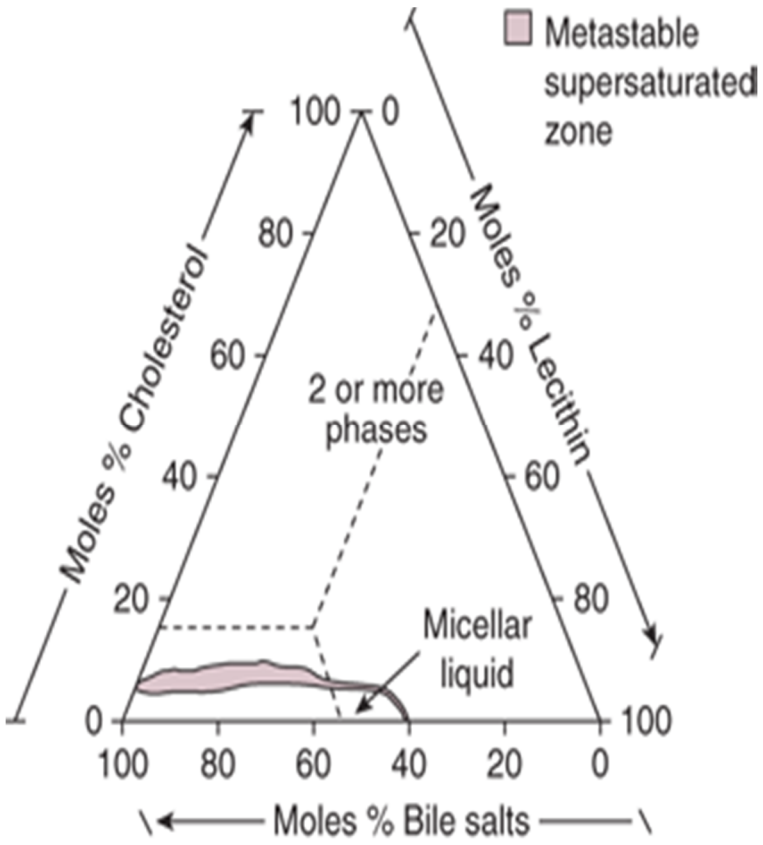


Figure 7 : Pathogenesis of gall stone formation

CHOLESTEROL STONES:

Pure cholesterol stones count for <10% of gallstones they usually contain variable amounts of bile pigments and calcium along with >70% cholesterol. They are usually soft , multiple and may be faceted or irregular. The colour varies according to the composition of cholesterol from yellow to green black . Cholesterol stones are radiolucent with <10% being radiopaque. Superstauration of bile with cholesterol is the main pathology in the formation of cholesterol stones. Dyslipidemia and cholesterol stone formation are strongly linked. Cholesterol is secreted into bile as cholesterol-phospholipid vesicles. and is her in solution by micelles which are a conjugated bile salt-phospholipid-cholesterol complex. Incorporation of vesicular lipids into micelles leads to vesicular maturation . Therefore, vesicles may become enriched in cholesterol and lead to formation of nucleated cholesterol crystals. In the supersaturated bile, cholesterol dense zones develop leading to the formation of cholesterol crystals.[13,15]

Figure 8 : Cholesterol stones

PIGMENT STONES:

Pigment stones may be black or brown pigment stones. Black pigment stones are usually small and sometimes spiculated. They contain <20% cholesterol. They are composed of calcium bilirubinate, calcium carbonate, and phosphate. Hemolytic disorders such as hereditary spherocytosis , sickle cell disease and cirrhosis lead to the formation of black pigment stones. Excess of conjugated bilirubin in hemolytic states leads to an increased rate of production of unconjugated bilirubin. Increased levels of Unconjugated bilirubin in bile precipitate calcium bilirubinate . Black stones are much more common in in Asian countries such as Japan, than in the Western hemisphere.

Brown stones are usually brownish yellow, soft, and small (<2cm). They are usually secondary to bacterial infection caused by bile stasis in either the gall bladder or bile ducts. Bacterial cell bodies and precipitated calcium bilirubinate form a major part of the stone. β-glucuronidase secreted by bacteria such as Escherichia coli enzymatically cleaves bilirubin glucuronide to produce the insoluble unconjugated bilirubin which in turn precipitates with calcium, and dead bacterial cell bodies to form brown stones in the biliary tree.[13,14 ,32]

Figure 9 : Pigment stones

CHOLEDOCHOLITHIASIS:

Common bile duct stones are usually formed within the gallbladder and migrate down the cystic duct to the common bile duct. De novo common bile duct stones are usually rare and occur post cholecystectomy . They are classified as secondary common bile duct stones and primary stones that form in the bile ducts. The primary stones are usually of the brown pigment type whereas the secondary stones are usually cholesterol stones. [15]

DIAGNOSTIC MODALITIES IN GALLS TONE DISEASE:

For several years oral cholecystography remained the investigation of choice for gallstones. In the 1950s, biliary scintigraphy , intrahepatic and endoscopic retrograde cholangiography (ERC), allowed for imaging of the biliary tract.

The advent of Ultrasonography, Magnetic resonance imaging and CT revolutionise the imaging of biliary tract and have remained the standard in diagnosis of biliary tract pathology.

ORAL CHOLECYSTOGRAPHY:

Oral cholecystography has mostly been replaced by ultrasonography in the diagnosis is gall stone disease. It involves oral administration of a radiopaque material that is excreted by the biliary tree into the gallbladder . Stones are visualised as filling defects

ULTRASONOGRAPHY :

An ultrasound remains the initial investigation of choice for suspected biliary tree pathology as it is non-invasive, painless, avoids unnecessary radiation exposure and can be performed on critically ill patients. It is operator dependant . However its use is limited in obese patients, patient with ascites and distended bowel loops or gaseous abdomen. Ultrasound has a sensitivity and specificity of >90% in detecting gall stones. Stones reflect the ultrasound waves back to the ultrasonic transducer and cast an acoustic shadow allowing for easy identification. Polyps can also be identified when calcified as they cast shadows but remain static. Sludge or debris can be picked up. Pericholecystic fluid, thickened oedematous gall bladder wall can be picked up on ultrasound. Chronic cholecystitis is usually detected by the presence of contracted thick walled gallbladder.

Ultrasonography is also useful in delineating the common bile duct anatomy. Proximal and mid portion of common bile duct is usually well visualised. Distal portion is usually obscured by bowel gas. Dilatation of common bile duct of more than 7mm is indicative of distal obstruction. Porcelain gall bladder and adenomyomatosis gall bladder can also be detected on ultrasound.[16]

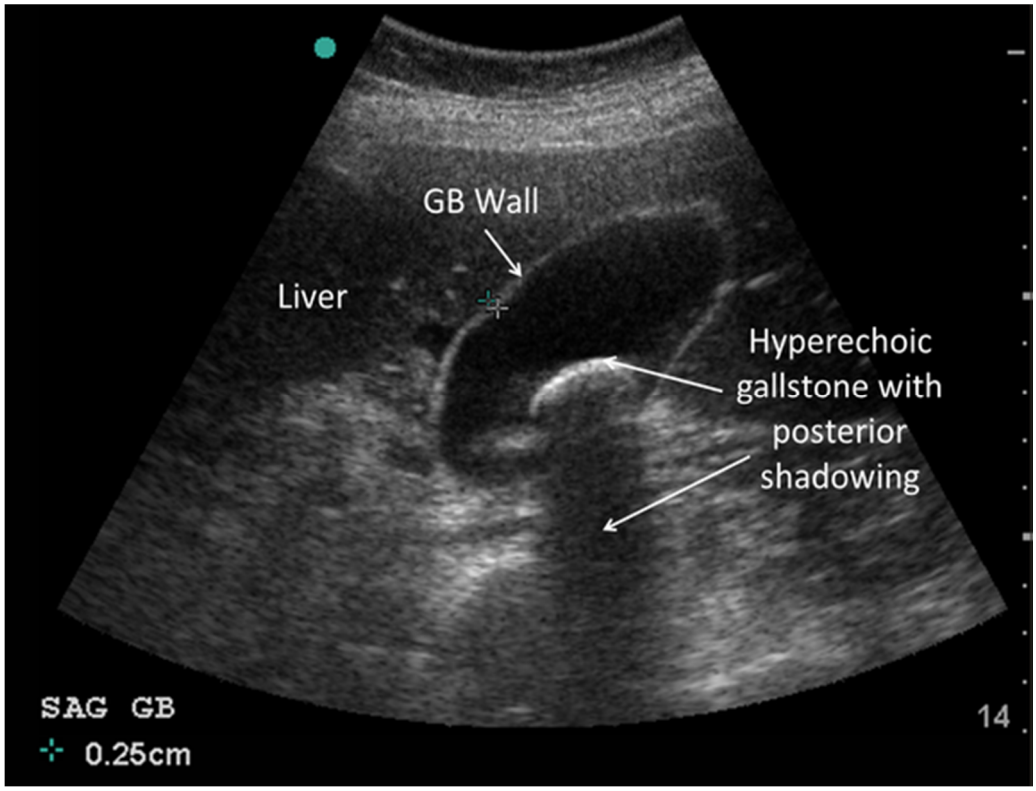


Figure 10 : Ultrasonography

BILIARY RADIONUCLIDE SCANNING (HIDA SCAN)

Biliary scintigraphy is a non- invasive method of evaluating the intraa and extra hepatic biliary system, gall bladder and duodenum .Hepaobiliary iminodiacetic acid (HIDA) is injected intravenously. It is then absorbed by the Kupffer cells in the liver, and excreted in the bile. In fasting subjects uptake by liver is detected in 10 minutes, the gallbladder, bile ducts, and duodenum are visualized within 60 minutes . Biliary scintigraphy is primarily used in the diagnosis of acute cholecystitis, which is seen as a non visualized gallbladder, with visualisation of the common bile duct and duodenum. On biliary scintigraphy cystic duct obstruction is highly diagnostic of acute cholecystitis. It has a 95% sensitivity and specificity . Gall bladder stasis and in patients receiving parenteral , false-positive results are seen. Delayed or absent filling of the duodenum with normal filling of gall bladder indicates an obstruction at the ampulla. Post- operative biliary leak can be localised in scintigraphy .

COMPUTED TOMOGRAPHY :

Computed tomography has its uses in diagnosis of gall bladder tumours, periampullary tumours and to delineate anatomy to provide a road map for surgery. However ultrasound has the advantage over CT in diagnosing the presence of cholelithiasis. [18]

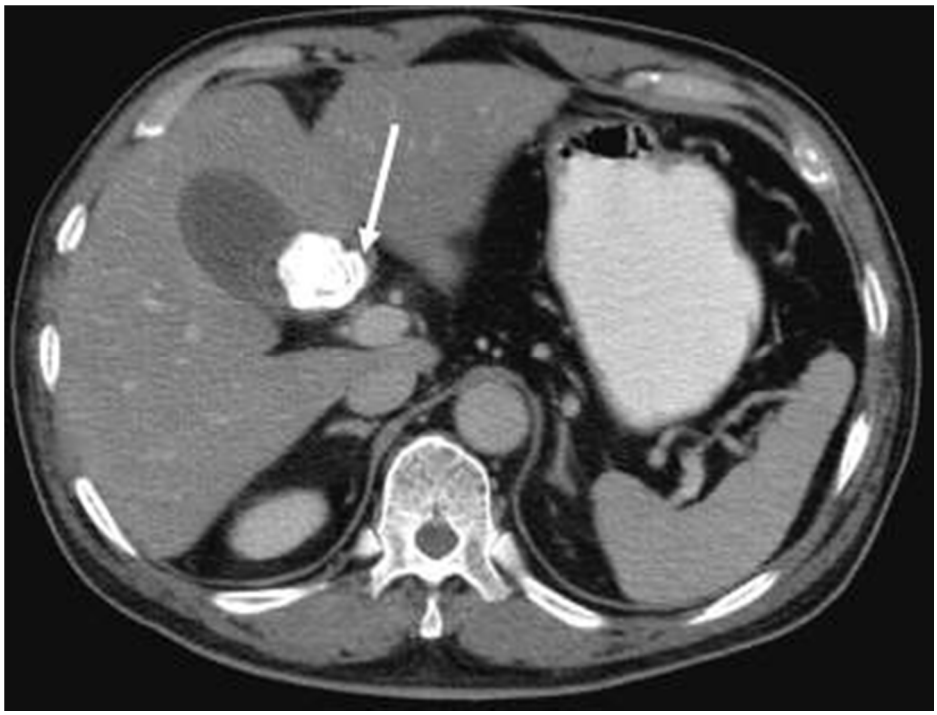


Figure 11 : CT abdomen

MAGNETIC RESONANCE IMAGING AND MAGNETIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

MRI and MRCP provide hi resolution images of Biliary anatomy as well as Pancreatic ducts. It has 95% sensitivity and 85% specificity in detecting gall stone disease. It can detect gall stones >5mm and distal stones which cannot be picked up by ultrasound. It the investigation of choice in most biliary tree pathologies . Patients requiring therapeutic interventions require endoscopic retrograde cholangiopancreatography. [19,20]

ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY :

ERCP allows for cannulation of the common bile duct in order to visualise the biliary tree anatomy using a side viewing endoscope. It carries the advantage of being therapeutic in addition to its diagnostic purpose. It is particularly useful in common bile duct stones, strictures and other bile duct pathologies. Sphincterotomy , common bile duct stone removal , stunting and biopsy can be performed through ERCP thus eliminating the need for invasive surgery. Pancreatitis , post ERCP cholangitis are some of the common complications encountered.[19,21]

Figure 12 : ERCP

ENDOSCOPIC ULTRASOUND

A special endoscope with an ultrasound transducer at the tip is used in endoscopic ultrasound. It provides non-invasive imaging of the biliary tree and allows from detecting of common bile duct stones <5mm. IT is also operator defendant like the ultrasound. It is useful in the evaluation of tumors and to delineate proximal biliary tree anatomy, nodal spread. It has the added advantage of being able to take biopsies of a tumor under ultrasonic guidance.[17]

PTC - PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY :

Intrahepatic bile ducts can be accessed under fluoroscopic guidance and the bile duct is cannulated using Seldinger's technique. Once the catheter is in situ, a cholangiogram can be performed. Biliary drain insertions and stent placements can also be placed in the same sitting. Percutaneous transhepatic cholangiography (PTC) is especially useful in patients with bile duct strictures and tumors, as it helps define the biliary tree anatomy. It has no role in uncomplicated gall stone disease. Percutaneous intra hepatic cholangiography carries a risk of bleeding, cholangitis, bile duct injury and leak [17,19]

SYMPTOMATIC GALLSTONE DISEASE:

ACUTE CHOLECYSTITIS :

PATHOGENESIS:

In >95% of the cases Acute cholecystitis occurs secondary to gall stones with Tumour contributing to <1% of the cases. Acalculous cholecytitis is usually associated with systemic disease. Obstruction of cystic duct with gallstone leads to distension and inflammation which is mediated by mucosal toxin lysolecithin, bile salts and platelet aggregating factor. Prostaglandin synthesis aggravates the inflammation. In 15% to 30% of patients. there is superimposed bacterial infection occurs In acute cholecystitis is characterised by thickened gall bladder wall and subserosal haemorrhages . There is thickening of gall bladder wall with multiple subserosal haemorrhages leading to a hyperaemic gall bladder and accumulation of pericholecystic fluid. The mucosa also undergoes patchy necrosis. Inflammation may resolve if the obstructing factor (i.e stone) is dislodged, but in severe cases there is progression of inflammation with necrosis and gangrene of gall bladder wall.

Acute gangrenous cholecystitis develops which may be complicated by abscess formation (empyema gall bladder). Ischemic gall bladder wall can perforate leading to perforation peritionitis. Occasionally the bacterial infection may be caused by gas producing organisms which results in an entity called Emphysematous gall bladder . [30,33]

CLINICAL MANIFESTATIONS:

Acute cholecystitis usually begins as an attack of biliary colic but with continuous pain that lasts for several days. Pain is usually in the right hypochondriac and may radiate to back or to the right shoulder. When infection supervenes, there is usually fever, nausea , vomiting. Features of peritonitis may be present in severe cases with perforation. On examination, patient may be febrile, toxic with Right upper quadrant tenderness. Inspiratory arrest on deep palpation near tip of 9th costal cartilage is usually characteristic of Acute cholecystitis (Murphy's sign) . Occasionally a mass may be palpable due to adherent omentum. [30,33]

DIAGNOSIS :

A complete hemogram may show mild to moderate leukocytosis. High white cell count (>20,000) is usually suggestive ion severe inflammatory pathology such as gangrenous cholecystitis or perforation peritonitis. Liver function tests may show elevation of serum bilirubin with elevation of transaminases and alkaline phosphatase. Common bile duct stones usually have grossly elevated conjugated bilirubin. Diabetic patients may have a delayed presentation and usually have higher mortality than the normal population.

Ultrasonography has high sensitivity and specificity (95%) in the diagnosis of acute cholecystitis. It can detect the present of stones (acoustic shadows) , thickening go gall bladder wall peri cholecystic fluid and focal probe tender-

ness. Biliary HIDA scan may be useful in atypical cases and calculus cholecystitis. Normal HIDA scan excludes acute cholecystitis. [17,19]

MANAGEMENT:

Initial management includes institution of appropriate antibiotic therapy (Second generation cephalosporins with metronidazole) covering both Gram negative aerobes as well as anaerobes.

Cholecystectomy is the treatment of choice for acute cholecystitis . Early surgery (48-72 hours) of presentation is preferred over interval cholecystectomy (6 weeks later) . Laparoscopic cholecystectomy is the preferred procedure, however in the setting of acute cholecystitis conversion rate are high (10-15%) . [34,38] If the patient presents later than 72 hours after the onset of symptoms a delayed internal cholecystectomy is preferred as immediate surgery is fraught with difficulties due to inflammatory adhesions and carries a significant risk of intra operative as well as post-operative morbidity. In those unfit for surgery Cholecystostomy may be performed under antibiotic cover. [33,34]

CHRONIC CHOLECYSTITIS :

Chronic cholecystitis is characterized by recurrent attacks of pain which develops when a stone obstructs the cystic duct, resulting in a progressive distension of the gallbladder resulting in increased tension in the gall bladder wall. The pathologic changes can vary from a normal gallbladder with minor chronic inflammation in the mucosa, to a shrunken, nonfunctioning gallbladder with

gross transmural fibrosis and adhesions to nearby structures. The mucosa may be normal or hypertrophied, but progressively becomes atrophied, with the epithelium protruding into the muscle coat, leading to the formation of the Aschoff- Rokitansky sinuses. [37]

CLINICAL MANIFESTATIONS:

Pain occurring after ingestion of a fatty meal with increase in cholecystokinin in response to duodenal intra luminal fat , classically presenting as biliary colic. However this is seen only in 50% of the patients . Pain is usually in the epigastrium and right upper quadrant and may radiate to back. Pain usually lasts for a few hours. Any pain lasting more than 24 hours is suggestive of acute cholecystitis. Other symptoms such as bloating , nausea or even vomiting may be the attacks of pain. Other cause of symptoms such as gastroesophageal reflux disease, peptic ulcer disease, irritable bowel disease, diverticular disease, renal calculi, liver diseases, myocardial pain and pleuritic pain must be excluded. [37]

DIAGNOSIS :

Diagnosis relies on accurate history consistent with biliary tract disease. Ultrasonography can help document the presence of cholelithiasis. IT can also provide other important information such as common bile duct dilatation, gall bladder polyps, thickened contracted gall bladder and porcelain gall bladder. Even in the absence of stones, presence of sludge is also consistent with biliary colic. [17]

MANAGEMENT:

Patient with symptomatic gall stone disease must undergo elective cholecystectomy. Diabetic patients particular are at a higher risk for progression to acute cholecystitis and need definitive intervention as early as possible. Pregnant women who cannot be managed surgically may be given lifestyle modifications and supportive treatment until definitive surgery can be performed. Laparoscopic cholecystectomy for symptomatic gall stones provides symptomatic relief in >90% of the patients. [34,37]

CHOLEDOCHOLITHIASIS:

6-12% of the patients with gall bladder stones have associated common bile duct stones. The incidence increases to 20-25% of the patients > 60 years of age. Common bile duct stones are usually formed within the gall bladder and migrate down to the common bile duct causing either partial or complete obstruction.They are called secondary common bile duct stones. Primary common bile duct stones are usually associated with biliary stasis and infection and occur >2 years port cholecystectomy. Common bile duct stone obstruction can be complicated by biliary pancreatitis or cholangitis. [42]

CLINICAL MANIFESTATIONS:

Common bile duct stones may be complicated by biliary pancreatitis or cholangitis, this usually manifests as rain in the epigastrium and right hypochondrium. It is accompanied by nausea and vomiting . Stones causing complete ob-

struction usually presents with progressive jaundice. Small stones which pass out can cause spontaneous resolution of symptoms. [42,43]

DIAGNOSIS :

Common bile duct stones causing impaction usually manifest as elevated bilirubin , alkaline phosphates and transaminases.

Ultrasonography is useful in detecting proximal common bile duct stones, dilated duct and intra hepatic biliary duct dilatation. Distal stones are obscured by bowel gas which makes their detection more difficult on ultrasound. Magnetic resonance cholangiography has higher sensitivity compared to ultrasound (95%) in detecting stone >5mm . However, Endoscopic cholangiography remains the gold standard in detecting common bile duct stones. It also has the advantage of therapeutic intervention when required with cannulation of common bile duct and stone removal. Endoscopic ultrasound is as effective as ERCP in detecting common bile duct stones. [42,43]

MANAGEMENT:

Preoperative endoscopic cholangiography or an intraoperative cholangiogram are useful in documenting common bile duct stones. ERCP , sphincterotomy and stone removal followed by a laparoscopic cholecystectomy is the preferred line of management. Laparoscopic common bile duct exploration via the cystic duct or through a choledochotomy allows for stone removal in the same sitting as cholecystectomy. A T tube is usually left in situ in case a choledochotomy is

performed. Endoscopic treatment is found to be associated with less morbidity and mortality particularly in patients over the age of 70 . [43,44]

SURGICAL INTERVENTIONS:

CHOLECYSTOSTOMY:

It is performed in patients who are unfit to undergo cholecystectomy but in whom intervention is required. The distended gall bladder is decompressed under radiological guidance by passing a catheter The catheter may be left in situ to drain the infected bile . It however carries an increased risk of cholangitis due to its invasive nature. [41]

LAPAROSCOPIC CHOLECYSTECTOMY:

With the advent of laparoscopic surgery, Laparoscopic cholecystectomy is one of the procedures which carries a distinct advantage over open surgery in terms of reduced morbidity and mortality. Rarely a difficult cholecystectomy with thickened contracted gall bladder or densely adherent clot's triangle may need conversion to open. However with laparoscopic cholecystectomy the rate of cystic duct stump leaks have marginally increased. [38,39,40]

OPEN CHOLECYSTECTOMY:

With the introduction of laparoscopic cholecystectomy the number of open cholecystectomy has drastically reduced. It is now performed under two settings, one during conversion of the laparoscopic cholecystectomy and two as a step during another surgery like pancreaticoduodenectomy. [38]

COMMON BILE DUCT EXPLORATION:

. The common bile duct is fluoroscopically visualised and the duct is irrigated. A choledochotomy is performed in the supraduodenal portion of the CBD with stay sutures in situ. the stone is retrieved usually through a longitudinal incision . A T tube is left in situ and the duct is closed with absorbable sutures . [44,46]

THYROID ANATOMY :

The adult thyroid gland is brown in color and firm in consistency and is located posterior to the strap muscles. The normal thyroid gland weighs approximately 20 g, but gland weight varies with body weight and iodine intake. The thyroid lobes are located adjacent to the thyroid cartilage and connected in the midline by an isthmus that is located just inferior to the cricoid cartilage. A pyramidal lobe is present in about 50% of patients. The thyroid lobes extend to the middle of the thyroid cartilage superiorly and lie adjacent to the carotid sheaths and sternocleidomastoid muscles laterally. The strap muscles (sternohyoid, sternothyroid, and superior belly of the omohyoid) are located anteriorly and are innervated by the ansa cervicalis (ansa hypoglossi). The thyroid gland is enveloped by a loosely connecting fascia that is formed from the partition of the deep cervical fascia into anterior and poste- rior divisions. The true capsule of the thyroid is a thin, densely adherent fibrous layer that sends out septa that invaginate into the gland, forming pseudolobules. The thyroid capsule is condensed into the posterior suspensory or Berry's ligament near the cricoid cartilage and upper tracheal rings. [1,47]

BLOOD SUPPLY :

The superior thyroid arteries arise from the ipsilateral external carotid arteries and divide into anterior and posterior branches at the apices of the thyroid lobes. The inferior Thyroid arteries arise from the Thyrocervical trunk shortly after their origin from the subclavian arteries. The inferior thyroid arteries trav-

el upward in the neck posterior to the carotid sheath to enter the thyroid lobes at their midpoint. A Thyroidea ima artery arises directly from the aorta or innominate in 1% to 4% of individuals to enter the isthmus or replace a missing inferior thyroid artery. The inferior thyroid artery crosses the recurrent laryngeal nerve (RLN), necessitating identification of the RLN before the arterial branches can be ligated. The venous drainage of the thyroid gland occurs via multiple small surface veins, which coalesce to form three sets of veins—the superior, middle, and inferior thyroid veins. The superior thyroid veins run with the superior thyroid arteries bilaterally. The middle vein or veins are the least consistent. The superior and middle veins drain directly into the internal jugular veins. The inferior veins often form a plexus, which drains into the brachiocephalic veins.[1,47]

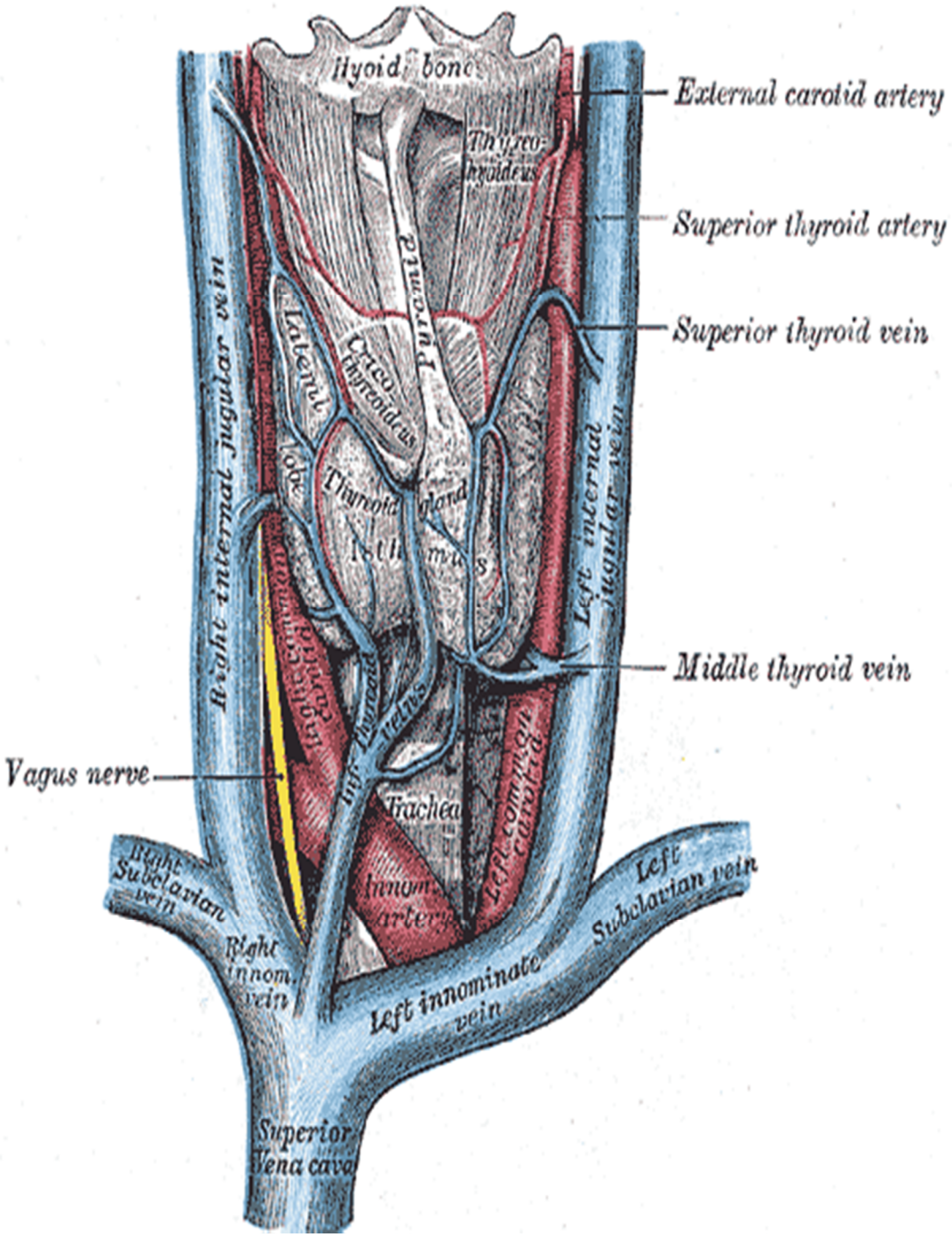


Figure 13 : Thyroid anatomy

NERVE SUPPLY :

The left RLN arises from the vagus nerve where it crosses the aortic arch, loops around the ligamentum arteriosum, and ascends medially in the neck within the tracheoesophageal groove. The right RLN arises from the vagus at its crossing with the right subclavian artery. The nerve usually passes posterior to the artery before ascending in the neck, its course being more oblique than the left RLN. Along their course in the neck, the RLNs may branch, and pass anterior, posterior, or interdigitate with branches of the inferior thyroid artery . The right RLN may be nonrecurrent in 0.5% to 1% of individuals and often is associated with a vascular anomaly. Non recurrent left RLNs are rare but have been reported in patients with situs inversus and a right-sided aortic arch. The RLN may branch in its course in the

1) Nerve in tracheoesophageal groove R: 64% L: 77%

2) Nerve lateral to trachea R: 28% L: 17%

3) Nerve far anterior neck, and identification of a small nerve should alert the surgeon to this possibility. Identification of the nerves or their branches often necessitates mobilization of the most lateral and posterior extent of the thyroid gland, the tubercle of Zuckerkandl, at the level of the cricoid cartilage. The last segments of the nerves often course below the tubercle and are closely approximated to the ligament of Berry. Branches of the nerve may traverse the ligament in 25% of individuals and are particularly vulnerable to injury at this

junction. The RLNs terminate by entering the larynx posterior to the cricothyroid muscle.

The RLNs innervate all the intrinsic muscles of the larynx, except the cricothyroid muscles, which are innervated by the external laryngeal nerves. Injury to one RLN leads to paralysis of the ipsilateral vocal cord, which comes to lie in the paramedian or the abducted position. The paramedian position results in a normal but weak voice, whereas the abducted position leads to a hoarse voice and an ineffective cough. Bilateral RLN injury may lead to airway obstruction, necessitating emergency tracheostomy, or loss of voice. If both cords come to lie in an abducted position, air movement can occur, but the patient has an ineffective cough and is at increased risk of repeated respiratory tract infections from aspiration.

The superior laryngeal nerves also arise from the vagus nerves. After their origin at the base of the skull, these nerves travel along the internal carotid artery and divide into two branches at the level of the hyoid bone. The internal branch of the superior laryngeal nerve is sensory to the supraglottic larynx. Injury to this nerve is rare in thyroid surgery, but its occurrence may result in aspiration. The external branch of the superior laryngeal nerve lies on the inferior pharyngeal constrictor muscle and descends alongside the superior thyroid vessels before innervating the cricothyroid muscle. Sympathetic innervation of the thyroid gland is provided by fibers from the superior and middle cervical sympathetic ganglia. The fibers enter the gland with the blood vessels and are vas-

omotor in action. Parasympathetic fibers are derived from the vagus nerve and reach the gland via branches of the laryngeal nerves. [1,47]

LYMPHATIC SYSTEM:

The thyroid gland is endowed with an extensive network of lymphatics. Intraglandular lymphatic vessels connect both thyroid lobes through the isthmus and also drain to perithyroidal structures and lymph nodes. Regional lymph nodes include pretracheal, paratracheal, perithyroidal, RLN, superior mediastinal, retropharyngeal, esophageal, and upper, middle, and lower jugular chain nodes. The central compartment includes nodes located in the area between the two carotid sheaths, whereas nodes lateral to the vessels are present in the lateral compartment. Thyroid cancers may metastasize to any of these regions, although metastases to submaxillary nodes (level I) are rare (<1%). There also can be "skip" metastases to nodes in the lateral ipsilateral neck without central neck nodes. [1,47]

THYROID HISTOLOGY

Microscopically, the thyroid is divided into lobules that contain 20 to 40 follicles . There ar about 3 · 10 follicles in the adult male thyroid gland. The follicles are spherical and average 30 μm in diameter. Each follicle is lined by cuboidal epithelial cells and contains a central store of colloid secreted from the epithelial cells under the influence of the pituitary hormone TSH. The second group of thyroid secretory cells is the C cells or parafollicular cells, which contain and secrete the hormone calcitonin. They are found as individual cells or

clumped in small groups in the interfollicular stroma and located in the upper poles of the thyroid lobes. [1,47]

THYROID PHYSIOLOGY:

Iodine Metabolism. The average daily iodine requirement is 0.1 mg, which can be derived from foods such as fish, milk, and eggs or as additives in bread or salt. In the stomach and jejunum, iodine is rapidly converted to iodide and absorbed into the bloodstream, and from there it is distributed uniformly throughout the extracellular space. Iodide is actively transported into the thyroid follicular cells by an adenosine triphosphate (ATP)–dependent process. The thyroid is the storage site of >90% of the body's iodine content and accounts for one third of the plasma iodine loss. The remaining plasma iodine is cleared via renal excretion.

THYROID HORMONE SYNTHESIS, SECRETION, AND TRANSPORT.

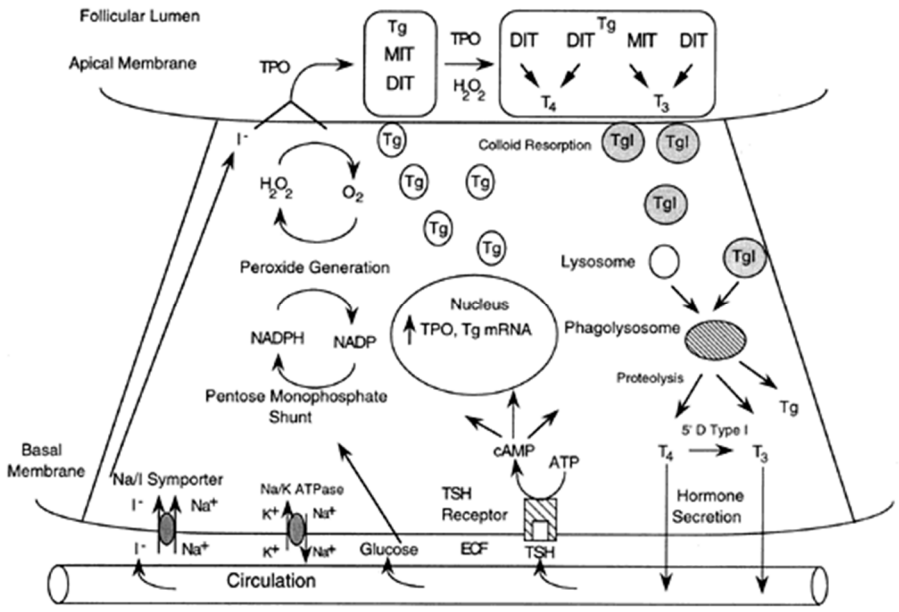


Figure 14 : Thyroid hormone synthesis

The synthesis of thyroid hormone consists of several steps (Fig. 38-8). The first, iodide trapping, involves active (ATP- dependent) transport of iodide across the basement membrane of the thyrocyte via an intrinsic membrane protein, the sodium/ iodine (Na/I) symporter. Thyroglobulin (Tg) is a large (660 kDa) glycoprotein, which is present in thyroid follicles and has four tyrosyl residues. The second step in thyroid hormone synthe- sis involves oxidation of iodide to iodine and iodination of tyrosine residues on Tg, to form mono iodotyrosines (MIT) and di iodotyrosines (DIT). Both processes are catalyzed by thyroid peroxidase (TPO). A recently identified protein, pendrin, is thought to mediate iodine efflux at the apical membrane. The third step leads to coupling of two DIT molecules to form tetra-iodothyronine or thyroxine (T4), and one DIT

molecule with one MIT molecule to form 3,5,3′-triiodothyronine (T3) or 3,3′,5′-triiodothyronine reverse (rT3). When stimulated by TSH, thyrocytes form pseudopodia, which encircle portions of cell membrane containing Tg, which in turn, fuse with enzyme-containing lysosomes. In the fourth step, Tg is hydrolyzed to release free iodothyronines and mono- and diiodotyrosines. The latter are deiodinated in the fifth step to yield iodide, which is reused in the thyrocyte. In the euthyroid state, T4 is produced and released entirely by the thyroid gland, whereas only 20% of the total T3 is produced by the thyroid. Most of the T3 is produced by peripheral deiodination (removal of 5′-iodine from the outer ring) of T3 in the liver, muscles, kidney, and anterior pituitary, a reaction that is catalyzed by 5′-mono-deiodinase. Some T4 is converted to rT3, the metabolically inactive compound, by deiodination of the inner ring of T4. In conditions such as Graves' disease, toxic multinodular goiter, or a stimulated thyroid gland, the proportion of T3 released from the thyroid may be dramatically elevated. Thyroid hormones are transported in serum bound to carrier proteins such as T4-binding globulin, T4-binding pre albumin, and albumin. Only a small fraction (0.02%) of thyroid hormone (T3and T4) is free (unbound) and is the physiologically active component. T3 is the more potent of the two thyroid hormones, although its circulating plasma level is much lower than that of T4. T3 is less tightly bound protein in the plasma than T4, and so it enters tissues more readily. T3 is three to four times more active than T4 per unit weight, with a half-life of about 1 day, compared to approximately 7 days for T4.

The secretion of thyroid hormone is controlled by the hypothalamic-pituitary-thyroid axis . The hypo- thalamus produces a peptide, the thyrotropin-releasing hormone (TRH), which stimulates the pituitary to release TSH or thyrotropin. TRH reaches the pituitary via the porto-venous circulation. TSH, a 28-kDa glycopeptide, mediates iodide trap- ping, secretion, and release of thyroid hormones, in addition to increasing the cellularity and vascularity of the thyroid gland. The TSH receptor (TSH-R) belongs to a family of G-protein– coupled receptors that have seven transmembrane spanning domains and use cyclic adenosine monophosphate in the signal- transduction pathway. TSH secretion by the anterior pituitary is also regulated via a negative feedback loop by T4 and T3. Because the pituitary has the ability to convert T4 to T3, the latter is thought to be more important in this feedback control. T3 also inhibits the release of TRH.

The thyroid gland also is capable of autoregulation, which allows it to modify its function independent of TSH. As an adaptation to low iodide intake, the gland preferentially synthesises T3 rather than T4, thereby increasing the efficiency of secreted hormone. In situations of iodine excess, iodide trans- port, peroxide generation, and synthesis and secretion of thyroid hormones are inhibited. Excessively large doses of iodide may lead to initial increased organification, followed by suppression, a phenomenon called the *Wolff-Chaikoff effect*. Epinephrine and human chorionic gonadotropin hormones stimulate thyroid hormone production. Thus, elevated thyroid hormone levels are found in pregnancy and gynaecologic malignancies such as hydatidiform mole. In contrast,

glucocorticoids inhibit thyroid hormone production. In severely ill patients, peripheral thyroid hormones may be reduced, without a compensatory increase in TSH levels, giving rise to the euthyroid sick syndrome.

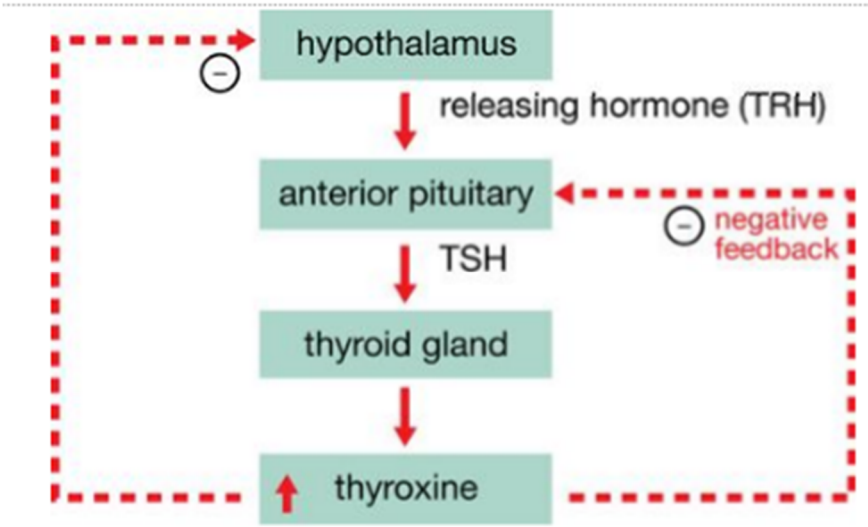


Figure 15 : Thyroid Hormone Function

THYROID HORMONE FUNCTION.

Free thyroid hormone enters the cell membrane by diffusion or by specific carriers and is carried to the nuclear membrane by binding to specific proteins. T4 is de iodinated to T3 and enters the nucleus via active transport, where it binds to the thyroid hormone receptor. The T3 receptor is similar to the nuclear receptors for glucocorticoids, mineralocorticoids, estrogens, vitamin D, and retinoic acid. In humans, two types of T3 receptor genes (α and β) are located on chromosomes 3 and 17. Thyroid receptor expression depends on peripheral concentrations of thyroid hormones and is tissue specific—the α form is abundant in the central nervous system, whereas the β form predomi-

nates in the liver. Each gene product has a ligand-independent, amino-terminal domain; a ligand-binding, carboxy terminal domain; and centrally located DNA-binding regions. Binding of thyroid hormone leads to the transcription and translation of specific hormone-responsive genes.

Thyroid hormones affect almost every system in the body. They are important for fetal brain development and skeletal maturation. T3 increases oxygen consumption, basal metabolic rate, and heat production by stimulation of Na/K ATPase in various tissues. It also has positive inotropic and chronotropic effects on the heart by increasing transcription of the Ca ATPase in the sarcoplasmic reticulum and increasing levels of β-adrenergic receptors and concentration of G proteins. Myocardial α receptors are decreased, and actions of catecholamines are amplified. Thyroid hormones are responsible for maintaining the normal hypoxic and hypercapnic drive in the respiratory center of the brain. They also increase gastrointestinal (GI) motility, leading to diarrhea in hyperthyroidism and constipation in hypothyroidism. Thyroid hormones also increase bone and protein turnover and the speed of muscle contraction and relaxation. They also increase glycogenolysis, hepatic gluconeogenesis, intestinal glucose absorption, and cholesterol synthesis and degradation. [50]

EVALUATION OF PATIENTS WITH THYROID DISEASE:

THYROID FUNCTION TESTS:

A multitude of different tests are available to evaluate thyroid function. No single test is sufficient to assess thyroid function in all situations, and the results must be interpreted in the context of the patient's clinical condition.

Serum Thyroid-Stimulating Hormone (Normal 0.5–5 μU/mL) The tests for serum TSH are based on the following principle: monoclonal TSH antibodies are bound to a solid matrix and bind serum TSH. A second monoclonal antibody binds to a separate epitope on TSH and is labeled with radioisotope, enzyme, or fluorescent tag. Therefore, the amount of serum TSH is proportional to the amount of bound secondary antibody (immunometric assay). Serum TSH levels reflect the ability of the anterior pituitary to detect free T_4 levels. There is an inverse relationship between the free T_4 level and the logarithm of the TSH concentration small changes in free T_4 lead to a large shift in TSH levels. The ultrasensitive TSH assay has become the most sensitive and specific test for the diagnosis of hyper- and hypothyroidism and for optimizing T_4 therapy.

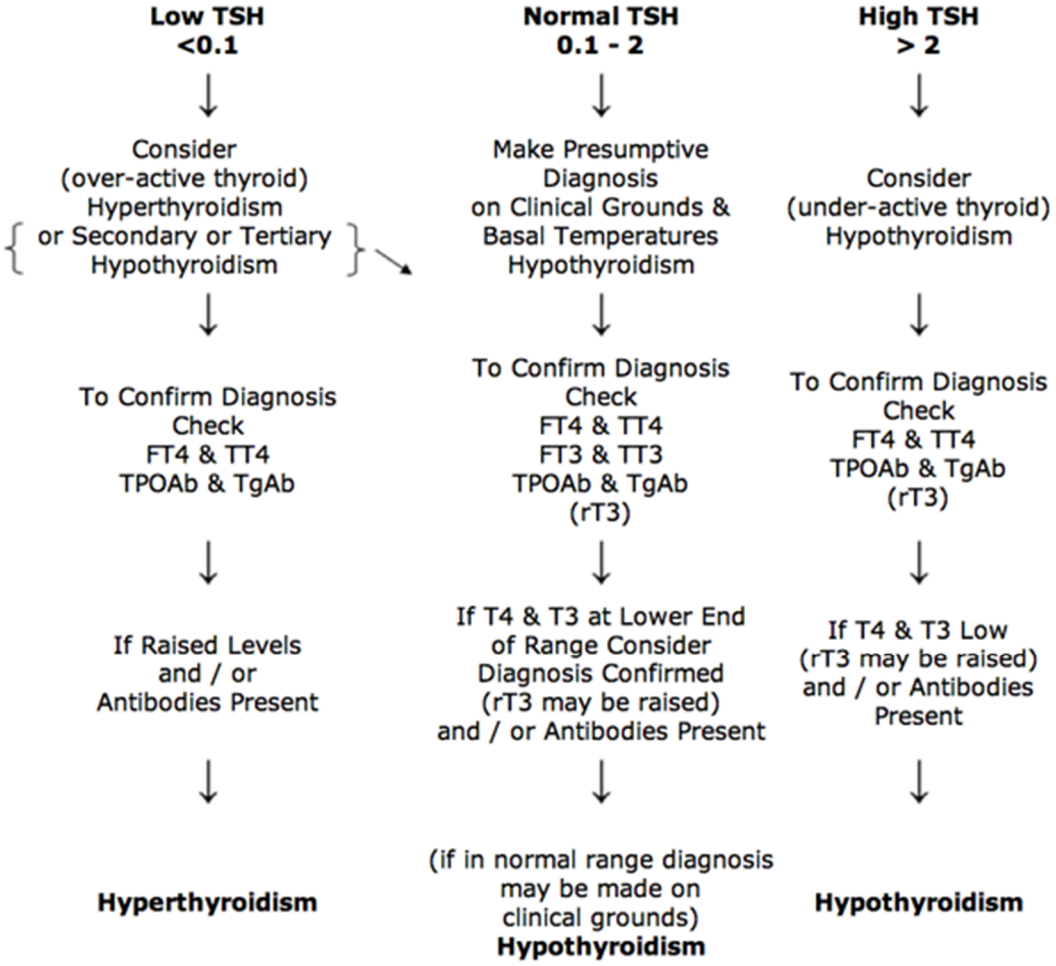


Figure : 16 Thyroid Hormone Function Test

Total T_4 (Reference Range 55–150 nmol/L) and T_3 (Reference Range 1.5–3.5 nmol/L) Total T_4 and T_3 levels are measured by radioimmunoassay and measure both the free and bound components of the hormones. Total T_4 levels reflect the output from the thyroid gland, whereas T_3 levels in the nonstimulated thyroid gland are more indicative of peripheral thyroid hormone metabolism, and are, therefore, not generally suitable as a general screening test. Total T_4 levels are increased not only in hyperthyroid patients, but also in those with elevated Tg levels secondary to pregnancy, estrogen/progesterone use, or con-

genital diseases. Similarly, total T_4 levels decrease in hypothyroid- ism and in patients with decreased Tg levels due to anabolic steroid use and protein-losing disorders like nephrotic syndrome. Individuals with these latter disorders may be euthyroid if their free T_4 levels are normal. Measurement of total T_3 levels is important in clinically hyperthyroid patients with normal T_4 levels, who may have T_3 thyrotoxicosis. As discussed previously in Thyroid Hormone Synthesis, Secretion, and Transport, total T_3 levels often are increased in early hypothyroidism.

Free T_4 (Reference Range 12–28 pmol/L) and Free T_3 (3–9 pmol/L) These radioimmunoassay-based tests are a sensitive and accurate measurement of biologically active thyroid hormone. Free T_4 estimates are not performed as a routine screening tool in thyroid disease. Use of this test is confined to cases of early hyperthyroidism in which total T_4 levels may be normal but free T_4 levels are raised. In patients with end-organ resistance to T_4 (Refetoff's syndrome), T_4 levels are increased, but TSH levels usually are normal. Free T_3 is most useful in confirming the diagnosis of early hyperthyroidism, in which levels of free T_4 and free T_3 rise before total T_4 and T_3. Free T_4 levels may also be measured indirectly using the T_3-resin uptake test. If free T_4 levels are increased, fewer hormone binding sites are available for binding radiolabeled T_3 that has been added to the patient's serum. Therefore, more T_3 binds with an ion-exchange resin, and the T_3-resin uptake is increased.

Thyrotropin-Releasing Hormone This test is useful to evaluate pituitary TSH secretory function and is performed by administering 500 μg of TRH intrave-

nously and measuring TSH levels after 30 and 60 minutes. In a normal individual, TSH levels should increase at least 6 μIU/mL from the baseline. This test also was previously used to assess patients with borderline hyperthyroidism but has largely been replaced by sensitive TSH assays for this purpose.

Thyroid Antibodies Thyroid antibodies include anti-Tg, antimicrosomal, or anti-TPO and thyroid-stimulating immunoglobulin (TSI). Anti-Tg and anti-TPO antibody levels do not determine thyroid function, but rather indicate the underlying disorder, usually an autoimmune thyroiditis. About 80% of patients with Hashimoto's thyroiditis have elevated thyroid antibody levels; however, levels may also be increased in patients with Graves' disease, multinodular goiter, and occasionally, thyroid neoplasms.

Serum Thyroglobulin Tg is only made by normal or abnormal thyroid tissue. It normally is not released into the circulation in large amounts but increases dramatically in destructive processes of the thyroid gland, such as thyroiditis, or overactive states such as Graves' disease and toxic multinodular goiter. Elevated anti- Tg antibodies can interfere with the accuracy of serum Tg levels and should always be measured when interpreting Tg levels. [51,52]

THYROID HORMONE AND CHOLESTEROL METABOLISM :

Thyroid hormones play an important role in cholesterol metabolism with over 50% of patients with overt hypothyroidism exhibiting dyslipidemia, particularly elevated low density lipoprotein levels (LDL). Early institution of thyroid hormone replacement has been shown to have positive effect on the lipid pro-

file. Hyperthyroid patients may have reduced expression of the LDL receptor gene thus having reduced LDL receptor activity leading to reduced removal of cholesterol from the serum. Thyroid hormones also lead to an increased synthesis of cholesterol by up-regulation HMG-CoA reductase.[70] The effect of thyroid hormones on cholesterol-7-hydroxylase directly affects bile salt synthesis and hypothyroid patients have been shown to have a decrease in biliary bile salt concentration . Biliary secretion of cholesterol is also reduced in hypothyroidism . Thus increase in serum cholesterol levels leads to supersaturation of bile with cholesterol resulting in the formation of gallstones. [55,54]

MECHANISM OF GALLSTONE FORMATION IN PATIENTS WTH HYPOTHYROIDISM:

The pathogenesis of gallstones involve various mechanisms that affect bile content and bile flow. The evidence of the effects of hypothyroidism on Gall stones and CBD stones formation has been proven by recent studies. IT can postulated that risk for gallstones in hyperthyroid patient is increased.

In hypothyroidism, the reduced levels of thyroxine decreases liver cholesterol metabolism and increases serum cholesterol levels resulting in supersaturation of bile which results in the formation of cholesterol crystals and ultimately to the nucleation and formation of gallstones. [70]

Low thyroxine also reduces bile secretion from hepatocytes and impairs clearance of precipitates from the bile ducts.

Thyroid hormone has a direct effect on Sphincter of Oddi relaxation resulting in delayed bile flow , stasis and formation of gallstones.

In humans, the Sphincter of Oddi expresses both TR β1 and β2 which are responsive to thyroid hormone stimulation and relax in response. [55,54]

REDUCED BILE FLOW IN DUODENUM IN HYPOTHYROID PATIENTS

In animal model studies hypothyroidism was found to reduce the bile flow into the duodenum. Similarly, in a prospective human study, hepatic clearance was found to be significantly decreased and the transit time from hilum-duodenum was increased in the hypothyroid patients. This supports the theory that bile flow into the duodenum is reduced in the hypothyroid stage which could be due to changes in both gall bladder motility and bile composition and also due to changes in the sphincter of Oddi pressure. [58,59]

THYROXINE AND ITS EFFECT ON SPHINCTER OF ODDI FUNCTION :

Gastrointestinal hypoactivity in hypothyroidism has been well established. Thyroid hormones have a direct pro relaxant effect on vascular smooth muscle contractility which is mediated by intra nuclear binding of Thyoid hormone to the receptor, and partly by non genomic mechanisms involving extranuclear sites of action. In a study conducted by Sandblom et al. the hormonal action of cholecystokinin (CCK) on the Sphincter of Oddi has been demonstrated . In

addition several hormones have been shown to have an effect on Sphincter of Oddi activity. Thyroxine has been found to have a direct effect on Sphincter of Oddi contractility in physiological concentrations in pig experiments. Triiodothyronine also had a similar effect on thyroxine in in vitro experiments. Thyroxine however was found to have an effect on only the histamine and acetylcholine induced sphincter of oddi contraction. It did not affect KCl mediated contractions. Thus in hypothyroidism reduced thyroxine and loss of its pro relaxant effect which holds clinical significance in cholestasis and subsequent formation of gall stones .

Studies have shown that Human Sphincter of Oddi was found to express Thyroxine Receptors β1 and β2. The evidence of Thyroxine Receptors in the Sphincter of Oddi is however sufficient evidence to conclude that thyroxine exerts a direct prorelaxant effect via a hormone-receptor complex action. The have also demonstrated that the underlying cellular mechanisms involved require a certain time lag, partially supporting the theory of the action of thyroxine mediated sphincter of Oddi relaxation. The pro relaxant effect of thyroxine on the sphincter is partly mediated by transporter proteins, and partly by nuclear receptors which leads to the activation of K+ channels. [54, 70]

PREVALENCE OF HYPOTHYROIDISM IN GALL STONE DISEASE PATIENTS:

Various recent studies report an association between hypothyroidism, and subclinical hypothyroidism, and gall stones. This finding suggested that factors

such as thyroxine effect on cholesterol metabolism and additional factors such as thyroxine effects on bile flow may also contribute to gall stone formation. In a retrospective study on patients over the age of 60 , it was noted that CBD stones were more commonly diagnosed in hypothyroidism (11%), when compared to control patients without gallstones(2%), and to isolated gallbladder stone patients (6%) [67] .A prospective study revealed a higher prevalence of subclinical hypothyroidism among gall stone patients. This study revealed the higher prevalence of undiagnosed subclinical hypothyroidism in euthyroid patients with common bile duct stone patients compared to patients with no gallstones. It was found that 5.3% of the gall stone patients had subclinical hypothyroidism, with serum TSH above the upper normal limit, compared to only 1.4% in the controls. In women over the age of 60 years, the prevalence of subclinical hypothyroidism was around 11.4% in patients with gall stones as opposed to 1.8% among the patients without gall stones. A large volume study conducted in Finland in 2010 confirmed the higher prevalence of hypothyroidism in gall stone disease patients. The prevalence of gall stone disease was studied in patients with proven hypothyroidism and correlated with age, sex, and area of residence of the patients. Only purely hypothyroid patients were included with exclusion of other co morbid conditions. Of the 14,334 patients studied , 0.23% in the hypothyroid cohort and 0.16% in the control cohort had associated gall stones disease requiring treatment . Following diagnosis there were 56% more gall stone treatments among the individuals in the hypothyroid cohort compared to the control cohort. Untreated hypothyroidism over a pro-

longed period of time explains the time taken for stone formation which may have begun during the untreated period of hypothyroidism. This correlates with the older age group in which hypothyroidism and gall stone disease are prevalent together. This hypothesis is also supported by the finding that subclinical and clinical hypothyroidism are more prevalent among gall stone patients. [70] The question remains whether thyroxine replacement therapy can cause reversal or halt the stone formation process . Certain studies have demonstrated the dissolution of gall stones following administration of thyroid hormone replacement. However they are smaller case reports and no large scale clinical trials have supported this hypothesis. Early institution of thyroid replacement theory has however demonstrated a proven positive effect on cholesterol metabolism. These findings further help strengthen the temporal association between hypothyroidism and gall stone disease. [54, 69, 70]

MATERIALS AND METHODOLOGY

STUDY POPULATION: 50 inpatients with radiologically proven gallstone disease in PSG hospitals Coimbatore.

INCLUSION CRITERIA:

Patients aged 20-80 with proven Gallstone disease (Ultrasonography/CECT/ERCP)

EXCLUSION CRITERIA:

Patients un willing for study

Patients <20 - >80 years

SAMPLE SIZE: A convenient sample size of 50 patients to taken.

METHODOLOGY:

After obtaining informed consent, history (symptoms of hypothyroidism) will be taken

- ➢ Blood sample will be taken to perform Thyroid function tests
- ➢ Results will be tabulated along with ultrasonography findings

STUDY DESIGN : Prospective observational study

STATISTICAL ANALYSIS

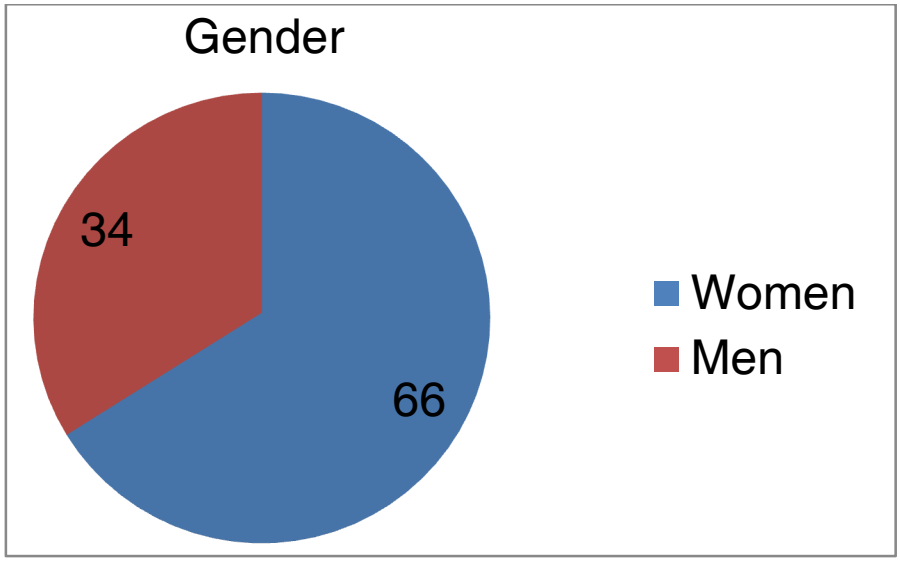
Data collected were entered in Excel Spread sheet and analyzed using STATA statistical software package release 11. We used the two-sided independent- samples t test to compare means across dichotomous variables (i.e. men v. women); the one-way ANOVA test for comparison of means across multilevel variables. Simple calculations like Percentages, Proportions and Mean values were derived. A type I error of 0.05 was considered in all analyses.

RESULTS AND DISCUSSION

A prospective study was conducted on the Prevalence of hypothyroidism in patients with proven Gall stone disease in a total of 50 patients in PSG institute of medical sciences and research, coimbatore from the period of October 2016 to August 2018. All patients who fit the inclusion criteria were evaluated clinically and Thyroid function test was performed. The results of the study are tabulated as follows .

Table 1 : Gender distribution

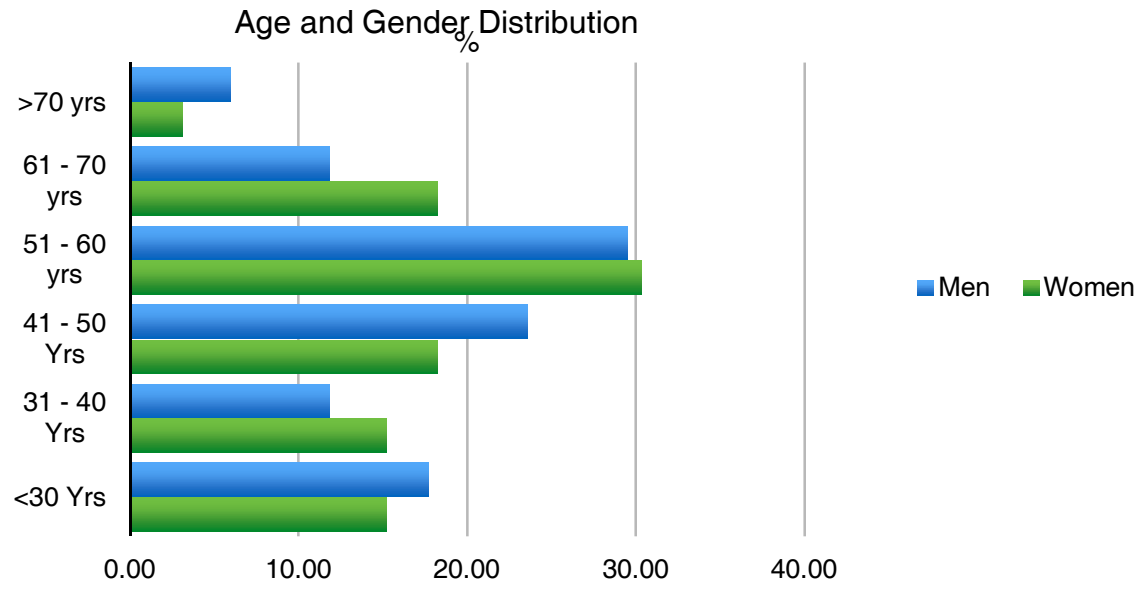
Gender	Freq.	Percent
Women	33	66
Men	17	34
Total	50	100



Of the 50 patients, 33 (66%) were women and 17 (34%) were men.

Table 2: Age and Gender distribution

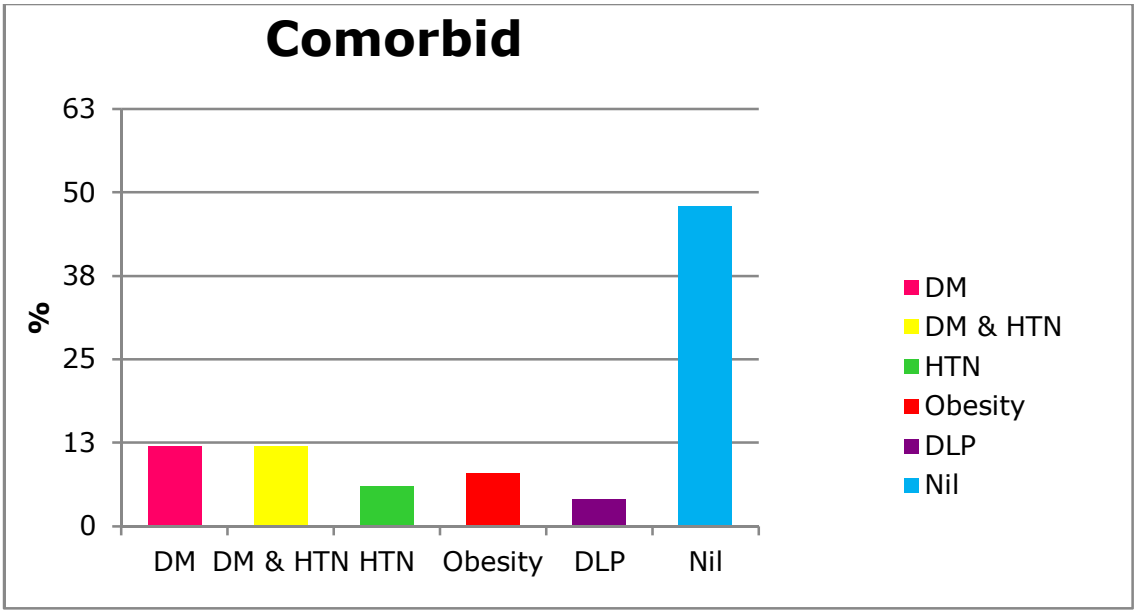
Age	Women		Men		Total	
	N	%	N	%	N	%
<30 Yrs	5	15.15	3	17.65	8	16.00
31 - 40 Yrs	5	15.15	2	11.76	7	14.00
41 - 50 Yrs	6	18.18	4	23.53	10	20.00
51 - 60 yrs	10	30.30	5	29.41	15	30.00
61 - 70 yrs	6	18.18	2	11.76	8	16.00
>70 yrs	1	3.03	1	5.88	2	4.00
Total	33		17		50	



The man age was 48.54. The ratio of female to male distribution is 1.9:1.

Table 3: Co morbidities in study population

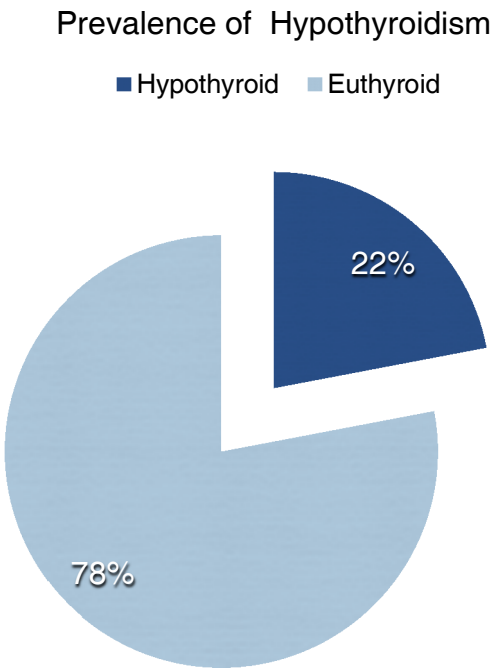
Comorbid	Freq.	Percent
DM	6	12
DM & HTN	6	12
HTN	3	6
Obesity	4	8
DLP	2	4
Nil	24	48
Total	50	100



Diabetes was the most common co morbidity followed by obesity (BMI >30) and hypertension.

Table 4: Prevalence of Hypothyroidism

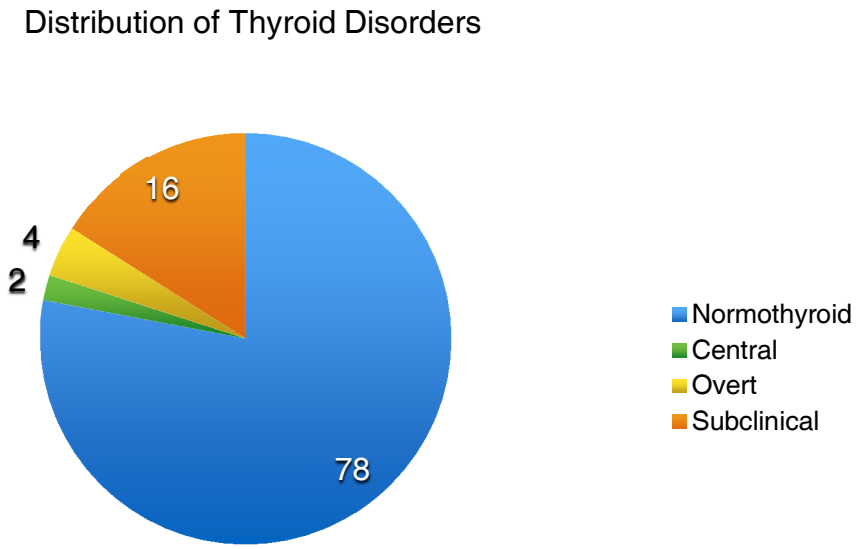
Prevalence	N	%
Hypothyroid	11	22
Euthyroid	39	78



Of the 50 patients, 11 (22%) were hypothyroid and 38 (78%) were euthyroid.

Table 5: Subclinical ,overt and central hypothyroidism

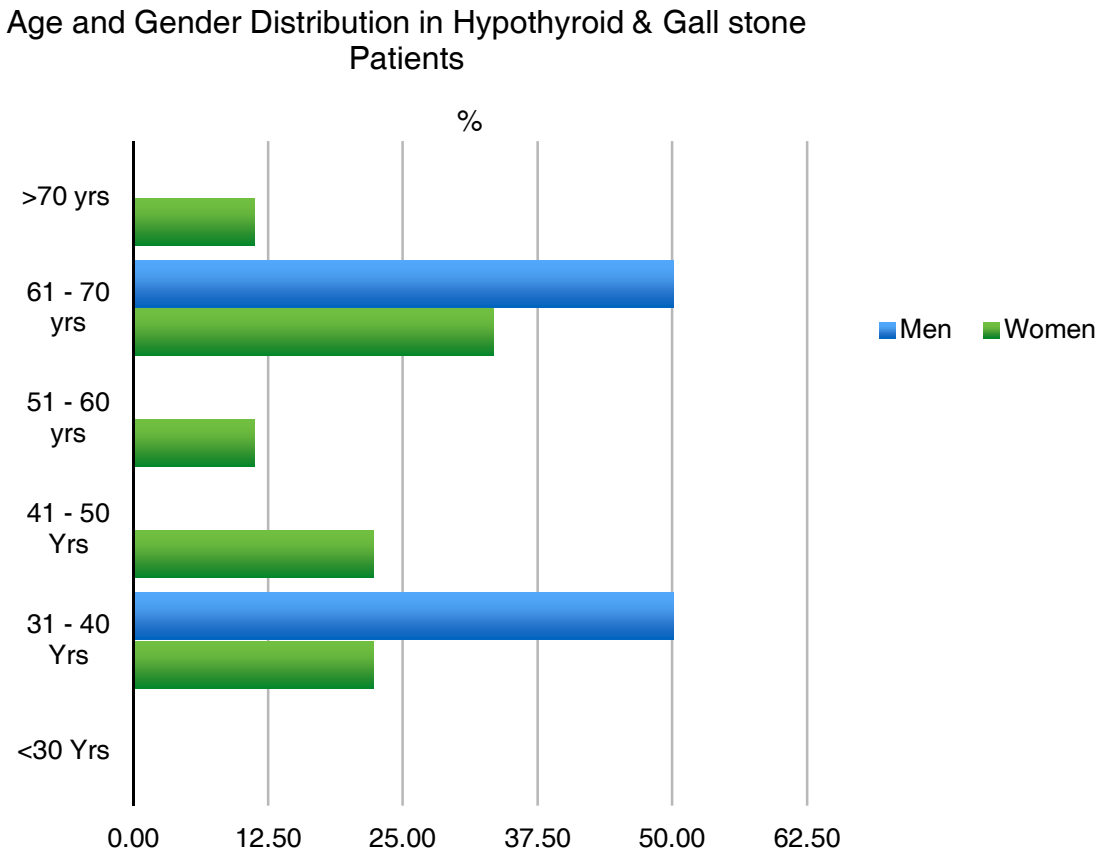
Condition	Number	Percentage
Euthyroid	38	78
Hypothyroid	11	22
Central	1	2
Overt	2	4
Subclinical	8	16



Of the hypothyroid patients, 8 (16%) were subclinical hypothyroidism, 2(4%) had overt hypothyroidism and 1 had central hypothyroidism.

Table 6: Age and gender distribution in patients with hypothyroidism and Gall stone disease

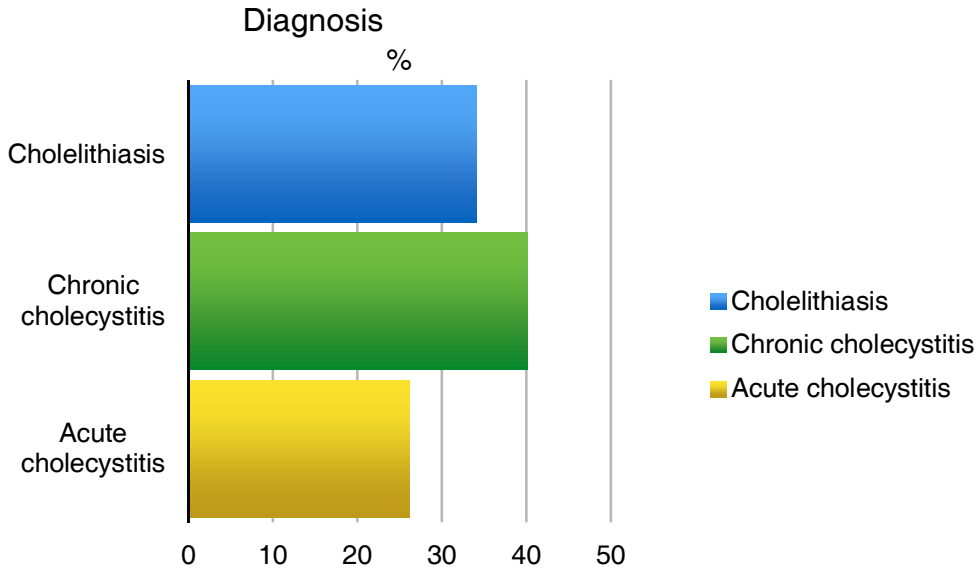
Age	Women		Men		Total	
	N	%	N	%	N	%
<30 Yrs	0	0.00	0	0.00	0	0.00
31 - 40 Yrs	2	22.22	1	50.00	3	27.27
41 - 50 Yrs	2	22.22	0	0.00	2	18.18
51 - 60 yrs	1	11.11	0	0.00	1	9.09
61 - 70 yrs	3	33.33	1	50.00	4	36.36
>70 yrs	1	11.11	0	0.00	1	9.09
Total	9		2		11	



The commonest age distribution in men and women with hypothyroidism and Gall stone disease was 61-70 years followed by 41-50 years in both sexes.

Table 7: Presentation and diagnosis

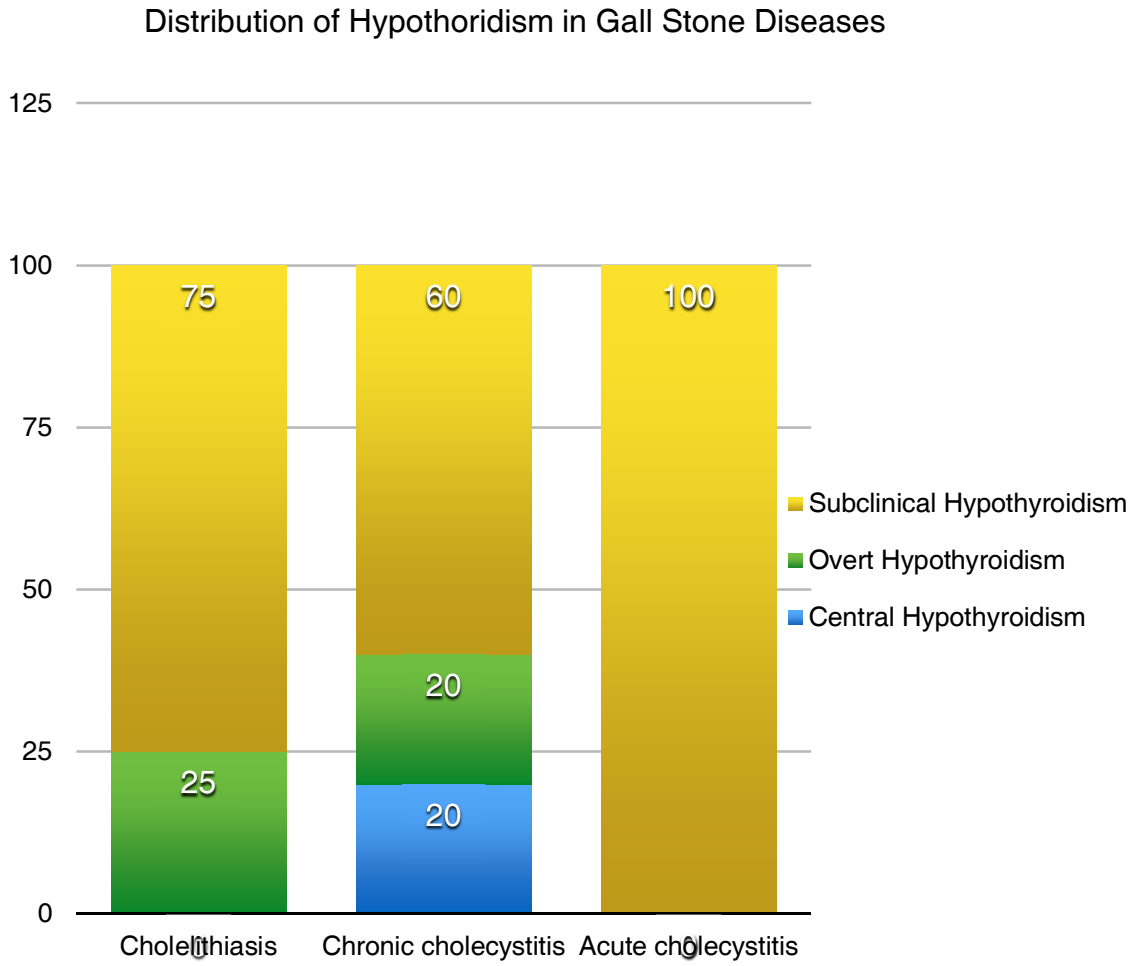
Diagnosis	Freq.	Percent
Acute cholecystitis	13	26
Chronic cholecystitis	20	40
Cholelithiasis	17	34
Total	50	100



Chronic cholecystitis (40%) was the commonest presentation in the study population followed by asymptomatic / Symptomatic cholelithiasis (34%) and Acute cholecystitis (26%) .

Table 8 : Distribution of hypothyroidism in Gall stone diseases

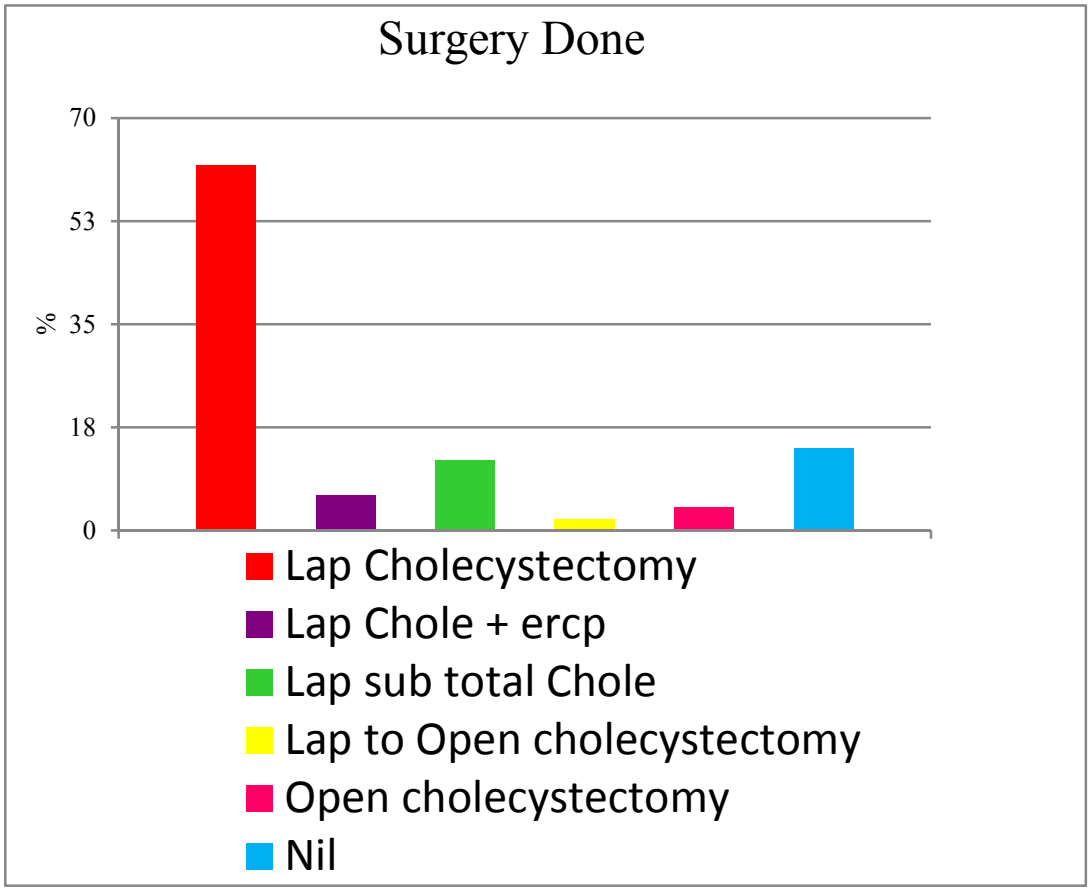
	Acute cholecysti-tis		Chronic chole-cystitis		Cholelithiasis		Total	
Hypothy-oidism	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Central	0	0	1	20	0	0	1	9
Overt	0	0	1	20	1	25	2	18
Subclinical	2	100	3	60	3	75	8	73
Total	2		5		4		11	



All patients who presented with Acute cholecystitis had sub clinical hypothyroidism. Where as those who presented with Chronic cholecystitis had predominantly subclinical hypothyroidism with equal percentages of overt and central hypothyroidism . Those with cholelithiasis were 75% sub clinical hypothyroidism and 25% overt hypothyroidism.

Table 9 : Interventions

Surgery Done	Freq.	Percent
Lap Chole	31	62
Lap Chole ercp	3	6
Lap sub tot Chole	6	12
Lap to Open chole	1	2
Open cholecystectomy	2	4
Nil	7	14
Total	50	100



Of the 50 patients , 62% underwent a laparoscopic cholecystectomy , 12% underwent a Laparoscopic subtotal cholecystectomy , 4% underwent an Open cholecystectomy and a 2% conversion rate from Laparoscopy to open Cholecystectomy.

DISCUSSION

A prospective study was conducted on the Prevalence of hypothyroidism in patients with proven Gall stone disease in a total of 50 patients in PSG institute of medical sciences and research, coimbatore from the period of October 2016 to August 2018. All patients who fit the inclusion criteria were evaluated clinically and Thyroid function test was performed.

SEX AND AGE WISE DISTRIBUTION :

Of the 50 patients, 33 (66%) were women and 17 (34%) were men. The ratio of female to male distribution is 1.9:1 making females the predomiant group . This is due to the higher prevalence of both hypothyroidism and gall stone disease in the female sex, influenced by multiple hormonal factors. The commonest age distribution in men and women with hypothyroidism and Gall stone disease was 61-70 years followed by 41-50 years in both sexes. The mean age was 48.54. A study by Singh BR et al reported a Male to female ratio in this study was 1:5.25. A study by Bansal et al found 65% females and 35% males in their study of 104 patients. [76]

COMORBID CONDITIONS:

Diabetes was the most common co morbidity (12%) ,12% had both Diabetes and hypertension followed by obesity (BMI >30) (8%) and hypertension (6%). This is predominantly due to metabolic syndrome in these patients as most of

these patients were also obese predisposing them to both gall stone disease due to deranged cholesterol metabolism and Diabetes mellitus . [74, 75]

PREVALENCE OF HYPOTHYROIDISM

Thyroid function tests were performed in all 50 patients, 11 (22%) were hypothyroid and 38 (78%) were euthyroid, in which 8 (16%) were subclinical hypothyroidism, 2(4%) had overt hypothyroidism and 1 (2%) had central hypothyroidism.

A prevalence rate of 22% was seen in the study population which is consistent with the rates obtained by similar studies in India. A prevalence rate of 24% was obtained in a study conducted by Singh BR et al in Madhya Pradesh.[76] In a study conducted by Kotwal et al in Sikkim a prevalence rate of 14% was found. [68]

PRESENTATION OF GALL STONE DISEASE:

Chronic cholecystitis (40%) was the commonest presentation in the study population followed by asymptomatic / Symptomatic cholelithiasis (34%) and Acute cholecystitis (26%) . All patients who presented with Acute cholecystitis had sub clinical hypothyroidism. Whereas those who presented with Chronic cholecystitis had predominantly subclinical hypothyroidism with equal percentages of overt and central hypothyroidism . Those with cholelithiasis were 75% sub clinical hypothyroid and 25% overt hypothyroidism. [64]

SURGICAL INTERVENTIONS:

Majority of the study population needed surgical interventions (both laparoscopic and open) 62% underwent a laparoscopic cholecystectomy , 12% underwent a Laparoscopic subtotal cholecystectomy , 4% underwent an Open cholecystectomy and a 2% conversion rate from Laparoscopy to open Cholecystectomy.

CONCLUSION AND CLINICAL IMPLICATIONS

In conclusion, this study has demonstrated a significant prevalence of hypothyroidism, or subclinical hypothyroidism in patients with gall stones. The higher prevalence of hypothyroidism in gall stone patients changes in the cholesterol metabolism which influence stone formation as well as changes in the sphincter of Oddi pressures which may lead to stasis and stone formation. [54] It cannot be ascertained whether hypothyroid individuals post cholecystectomy have an increased risk too common bile duct stones. Long history of hypothyroidism not only predisposes to cholesterol stone with alterations in cholesterol metabolism but also pigment stones. As absence of thyroxine leads to failure of Sphincter of Oddi relaxation which in turn leads to stasis of bile which is an important predisposing factor to the formation of pigment stones. . Treatment of subclinical hypothyroidism has demonstrated a positive effect on the serum cholesterol levels and it can be assumed that patients at risk of forming gall stones due to subclinical hypothyroidism may also benefit from such early thyroid hormone replacement. In conclusion, patients with increased risk of gall stone formation would greatly benefit from thyroid function testing to rule out subclinical hypothyroidism. [66,69]

RECOMMENDATIONS :

On the basis of the findings of the study, the following recommendations can be made:

1. Thyroid profile should be a considered as a part of general workup in patients with cholelithiasis especially in female obese patients.

2. Proper evaluation and preoperative preparation in patients with hypothyroidism, anticipating complications associated with the condition.

3. Early institution of thyroid replacement therapy in patients with clinical hypothyroidism .

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STUDY PROFORMA

PREVALENCE OF HYPOTHYROIDISM IN PATIENTS WITH GALL STONE DISEASE.

1) IDENTIFICATION NO :

2) AGE :

3) SEX :

4) IP NO :

5) DATE OF ADMISSION :

6) DATE OF DISCHARGE :

7) WEIGHT (KG) :

8) HT(CM) :

9) BMI :

10) CLINICAL EXAMINATION :

11) DIAGNOSIS :

12) CO-MORBID CONDITIONS :

13) PERSONAL HABITS : SMOKING/ ALCOHOL

14) NUTRITIONAL STATUS :

15) CURRENT MEDICATIONS :

16) RADIOLOGICAL INVESTIGATIONS:

i) Ultrasonogram :

ii) CECT abdomen :

iii) ERCP :

17) THYROID FUNCTION TEST : T3, T4, TSH, FT3, FT4

ABBREVIATIONS:

GB	:	Gall bladder
SO	:	Sphincter of Oddi
TH	:	Thyroid hormone
TSH	:	Thyroid stimaulating hormone
T3	:	Tri iodothyronine
T4	:	Tetra iodothyronine
CT	:	Computed tomography
PTC	:	Percutaneous transhepatic cholangiography
MRCP	:	Magnetic retrograde cholangiopancreatography
ERCP	:	Endoscopic retrograde cholangiopancreatography

OP NO	IP NO	AGE	Sex	Diagnosis	USG finding	Co morbs	FT3	FT4	T3	TSH	clinical Hypothyroid	Overt hypothyroidism	Central hypothyroidism	allstone ty	Surgery Done
O09095533	I16038659	31	F	Chronic cholecystitis	Gall bladder partially distended and shows few calculi, largest measuring 1.4cm.	Morbid obesity	2.9	1.31	0.91	3.06	0	0	0	Pigment	Lap Chole
O10107937	I17002239	28	F	Chronic cholecystitis	Gall bladder is distended and shows multiple tiny calculi within(< 5mm).	Nil	2.47	1.2	0.87	2.48	0	0	0	Pigment	Lap Chole
O12038882	I16039442	67	F	Chronic cholecystitis	Gall bladder is distended shows calculus of size 5.6mm.	SHTN, OSA	3.4	1.34	1.37	4.24	1	0		Pigment	Lap Chole
O04007016	I17006737	53	F	Chronic cholecystitis	Gall bladder is distended with sludge and shows multiple tiny calculi.	DM, SHTN	2.52	1.14	1.07	2.52	0	0	0	Pigment	Lap Chole + ERCP
O16030062	I16034434	60	M	Chronic cholecystitis	Gall bladder shows multiple polyps in the neck and body, largest measuring 5mm.	Nil	2.91	1.1	1.07	2.4	0	0	0	Pigment	Lap Chole
O16036658	I17013882	54	F	Chronic cholecystitis	Gall bladde wall thickened with few tiny calculi (5-7mm)	STHN, PAH, OSA	2.83	1.18	1.09	0.712	0	0	0	Pigment	Lap Chole
O16055769	I16033882	40	F	Chronic cholecystitis	Gall bladder contracted and shows few calculi, largest measuring 12mm.	Morbid obesity	2.66	1.1	1.14	0.953	0	0	0	Pigment	Lap Chole
O16084010	I16038228	50	F	Acute on Chronic cholecystitis	Gall bladder distended shows multiple tiny calculi, largest measuring 3mm.	Morbid obesity	2.26	1.07	0.95	0.11	0	0	0	Pigment	Lap Chole
O16087744	I16039956	20	M	Chronic cholecystitis	Gall bladder partially distended with few calculi noted in neck region, 9.1mm	Morbid obesity	2.88	1.25	0.93	2.91	0	0	0	Pigment	Lap Chole + ERCP
O17003049	I17002059	65	F	Chronic cholecystitis	Gall bladder distended with multiple calculi with 16mm CBD stone	Nil	2.27	0.86	0.84	1.16	0	0	1	Pigment	Lap Chole
O16071124	I17006860	51	F	Chronic cholecystitis with cholesterolos	Gall bladder distended with multiple calculi	Nil	1.86	1.43	0.76	13.8	1	0	0	Pigment	Lap cholecystectomy
O17022832	I17012167	75	F	Acute on chronic cholecytitis	Contracted Gall bladder with 16mm calculus with wall thickness of 2 mm	SHTN, DLP	2.29	1.43	0.99	8.29	1	0	0	Pigment	Lap to Open chole
O16057776	I17023083	80	M	Chronic cholecytstits	Gall bladder distended and shows calculus of size 11mm.	CVA, SHTN,DLP	3.45	1.23	1.22	2.9	0	0	0	N/A	Nil
O17044608	I17025263	27	F	Chronic cholecystitis with cholesterolos	Gall bladder with mulitple calculi 5-6mm	Nil	2.85	1.47	1.02	2.75	0	0	0	Pigment	Lap cholecystectomy
O16079538	I16035999	63	F	Acute cholecytitis	Gall bladder distended and shows multiplle calculi, the largest measuring 7.5mm, Gall bladder wall thickening 8.8mm with pericholecystic fluid	SHTN	2.43	1.16	1.1	4.65	1	0	0	Pigment	Lap cholecystectomy
O16087469	I17003686	53	F	Cholelithiasis with empyema	Gall bladder appears overdistended and shows fer calculi largest measuring 2.0 cm	DM	2.34	1.28	1.07	2.8	0	0	0	Pigment	Lap subtotal cholecystectomy
O18007738	I18004020	54	F	Cholelithiasis with adenomyomatosis	Gall bladder is distended and shows sludge and calculus measuring 1.1cm with adenomyomatosis.	DM/SHTN	3.57	1.96	1.17	2.16	0	0	0	Pigment	Lap cholecystectomy
O15007191	I18003227	32	F	Cholelithiasis	Gall bladder shows multiple small calculi with sludge	Nil	2.58	1.28	0.94	7.71	1	0	0	N/A	Nil
O15059408	I18000526	35	M	Cholelithiasis	Gall bladder multiple calculi 5-6mm	Nil	2.18	1.6	0.68	1.92	0	0	0	Pigment	Lap cholecystectomy
O15020919	I18007022	42	F	Cholelithiasis with choledocholithiasis	Gall bladder shows multiple calculi largest measuring 8mm,CBD measures 10mm, appears dilated and shows few calculi in distal CBD largest measuring 7.7mm.		0.86	0.39	0.41	85.5	0	1	0	Pigment	Lap cholecystectomy with ERCP
O13040756	I18006436	49	F	Cholecystitis with mirzzi syndrome	The gall bladder is minimally distended and shows few calculi, largest measuring12 x 7.8mm	BA	1.79	1.57	0.88	3.69	0	0	0	Pigment	Open cholecystectomy
O02027603	I18006594	64	M	Cholelithiasis	The gall bladder is distended and shows multiple small calculi	DM/SHTN/CAD	1.78	1.28	0.68	4.47	1	0	0	Pigment	Open cholecystectomy
O18029219	I18014368	52	M	Chronic Cholecystitis	Gall bladder shows multiple small calculi, impacted at the neck.	DM	2.34	1.55	0.9	1.01	0	0	0	Pigment	Lap cholecystectomy

OP NO	IP NO	AGE	Sex	Diagnosis	USG finding	Co morbs	FT3	FT4	T3	TSH	clinical Hypothyroid	Overt hypothyroidism	Central hypothyroidism	allstone ty	Surgery Done
O18025744	I18012820	47	M	Chronic cholecystitis	Gall bladder is distended with sludge and shows multiple tiny calculi.	Nil	2.89	1.6	1.31	3.32	0	0	0	Pigment	Lap subtotal cholecystectomy
O18013234	I18010140	29	F	Chronic cholecystitis	Gall bladder shows multiple small calculi with sludge	Nil	2.6	1.88	0.89	0.445	0	0	0	Pigment	Lap cholecystectomy
O18007384	I18003812	55	M	Cholelithiasis	Gall bladder is overdistended and shows echogenic sludge with few tiny calculi within.	DM	2.01	1.4	0.61	1.53	0	0	0	Pigment	Lap sub total cholecystectomy
O18006502	I18004406	58	F	Acute calculus cholecystitis	Gall bladder appears distended and shows multiple calculi largest measuirng 1.1cm	DM	2.37	1.72	0.91	1.13	0	0	0	Pigment	Lap cholecystectomy
O18003511	I18004540	67	F	Acute on chronic cholecytitis	Gall bladder is distended and shows few calculi , few of the noted in neck region, largest measuring 1.0cm and shows minimal wall thickening	Nil	2.08	1.39	0.75	2.01	0	0	0	Pigment	Lap subtotal cholecystectomy
O18003488	I18019362	40	M	Chronic cholecystitis	Contracted Gall bladder with multiple calculus with wall thickness of 10 mm	Nil	2.53	0.65	0.79	24.68	0	1	0	Pigment	Lap cholecystectomy
O18034320	I18017220	24	M	Gangrenous cholecytitis	Gall bladder with multiple calculi with pericholecystic fluid	Nil	2.01	1.29	0.58	0.446	0	0	0	Pigment	Lap subtotal cholecystectomy
O18025287	I18012608	54	F	Acute cholecystitis (perforated GB)	Gall bladder distended with multiple calculi	Nil	3.41	1.47	0.53	3.41	0	0	0	Pigment	Lap cholecystectomy
O18033764	I18019231	48	F	Acute cholecystitis	Gall bladder partially distended and shows few calculi, largest measuring 8 mm	SHTN	2.62	1.04	1.41	9.75	1	0	0	Pigment	Lap cholecystectomy
O18026111	I18012968	69	M	Acute cholecystitis	Gall bladder minimally distended with few calculi (4.8mm)	CVA, DM, PVD	1.2	1.5	0.42	0.858	0	0	0	Pigment	Lap subtotal cholecystectomy
O18032435	I18016913	28	F	Acute cholecytitis	Gall bladder wall thickened with few tiny calculi (5-7mm)	Nil	1.77	1.97	0.62	1.25	0	0	0	Pigment	Lap cholecystectomy
O18027474	I18017690	65	F	Acute cholecytitis	Gall bladder distended with multiple calculi	DM/SHTN	3	1.58	1	2.27	0	0	0	Pigment	Lap cholecystectomy
O18034746	I18019246	28	F	Acute cholecytitis	Gall bladder distended with multiple calculi	Nil	1.93	1.45	0.85	0.704	0	0	0	Pigment	Lap cholecystectomy
O18036376	I18018902	65	F	Acute calculus cholecystitis	Gall bladder partially distended and shows few calculi.	DM	1.82	2.32	0.7	0.414	0	0	0	Pigment	Lap cholecystectomy
O15042267	I18019712	45	F	Cholelithiasis	Gall bladder shows multiple small calculi with sludge	Nil	2.58	1.63	1.19	1	0	0	0	Pigment	Lap cholecystectomy
O18037556	I18020934	32	F	Cholelithiasis	Gall bladder shows calculus of 5.1mm	Nil	3.35	1.54	1.62	4.84	1	0	0	Pigment	Lap cholecystectomy
O18042989	I18021480	59	F	Cholelithiasis with choledocholithiasis	Gall bladder contracted with multiple calculi with proximal CBD calculus 7mm	DM	1.55	1.42	0.59	2.41	0		0	Pigment	Nil
O18045542	I18022546	49	M	Cholelithiasis	Gall bladder distended with 1.4 cm calculus	SHTN	2.76	1.34	1.28	2.35	0	0	0	Pigment	Lap cholecystectomy
O18042890	I18021382	58	M	Cholelithiasis	Gall bladder is overdistended with multiple calculi largest 7 mm wall thickness 5 mm	Nil	2.02	1.7	0.69	2.26	0	0	0	Pigment	Nil
O18044678	I18022168	58	F	Cholelithiasis	Gall bladder shows1.1cm neck calculus	DM/SHTN	2.15	0.96	0.88	3.81	0	0	0	Pigment	Lap cholecystectomy
O10086736	I18022246	39	F	Acute cholecytitis	Gall bladder distended 4-5mm calculi	Nil	2.38	1.4	0.95	1.99	0	0	0	Pigment	Lap cholecystectomy
O18045622	I18022729	57	M	Cholelithiasis	Gall bladder distended shows few calculi largest 9 mm	DM/SHTN	2.54	1.2	0.93	2.43	0	0	0	Nil	Nil
O18045267	I18022716	44	M	Cholelithiasis	Gall bladder with multiple calculi wall thickness 0.2 cm	DM /SHTN	3.82	0.96	1.4	1.89	0	0	0	Pigment	Lap cholecystectomy
O18047642	I18023385	21	M	Cholelithiasis	Gall bladder neck region calculus 6x7 mm	Nil	2.33	1.28	0.82	0.702	0	0	0	Pigment	Nil
O18047596	I18023353	55	F	Cholelithiasis	Gall bladder shows multiple calculi largest 9mm	Nil	2.41	0.95	1.1	3.31	0	0	0	Pigment	Nil
O18046923	I18023502	47	M	Acute calculous cholecystitis	Gall bladder shows echo genie sludge with calculous of 6 mm	Nil	1.42	1.71	0.49	1.08	0	0	0	Pigment	Lap cholecystectomy
O18036498	I18023359	41	F	Acute cholecystitis	Gall bladder distended with 1.7 cm calculus	Nil	2.27	1.27	0.81	2.24	0	0	0	Pigment	Lap cholecystectomy